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SEDIMENTATION OF MOLECULES IN CENTRIFUGAL FIELDS

THE SVEDBERG

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Received September 30, 1933

The usual methods for the determination of molecular weights in solution based upon the measurement of osmotic pressure, boiling point, or freezing point are, in principle, only procedures for counting the number of solute particles in the solution. If the concentration of the solute is known, the mean particle mass or molecular weight may be calculated. The mass of the individual particle or molecule does not influence the phenomenon studied. These classical methods, therefore, do not give any information about the weights of the different molecular species eventually present in the solution under investigation, but merely give us an average value of the molecular weight taken across all the species.

At the present time the means at our disposal for the measurement of individual molecular masses are very limited. The mass spectrograph allows of determination of the relation between electrical charge and mass of the different molecular species in a beam of molecular rays. If the charge be known the individual molecular mass may be calculated. This method, however, is possible only in the case of relatively simple molecules in gases at low pressures. The study of band spectra has furnished valuable information concerning moments of inertia and intermolecular distances, but this method, too, is restricted to gaseous systems containing molecules built up of only a few atoms.

The lack of a reliable method for the determination of molecular weights and especially for the molecular weight analysis of high molecular organic substances such as the proteins, the carbohydrates, the hydrocarbons, etc., has been a serious hindrance to research in those fields. When staying as a visiting professor at the University of Wisconsin ten years ago, the present writer

tried to outline such a method. The technique was then developed in his laboratory at the University of Upsala. The procedure in question is based upon the measurement of the sedimentation of molecules in strong centrifugal fields.

The theory is fairly simple as long as we have to deal with electrically neutral molecules, e.g., proteins at the isoelectric point (1). Two different possibilities of measurement exist. We can determine the concentration gradient in a small column of solution exposed to the influence of the centrifugal field until equilibrium has been reached between sedimentation and diffusion (sedimentation equilibrium method). For each molecular species the following formula is valid:

$$M = \frac{2 RT \ln (c_2/c_1)}{(1 - V\rho)\omega^2(x_2^2 - x_1^2)} \quad (1)$$

where M = molecular weight,

R = gas constant,

T = absolute temperature,

V = partial specific volume of solute,

ρ = density of solvent,

x_2 and x_1 are distances to the center of rotation, and

ω = angular velocity.

An inhomogeneity with regard to molecular weight shows up as a drift in the values with distance from the center of rotation. The absence of drift is therefore a reliable criterion that only one species of molecules is present in the solution. In the case of more than one species of solute molecules it is often possible, by choosing different intensities of the centrifugal field, to get one or the other component to predominate at the top or at the bottom of the column of solution.

A still sharper test of homogeneity, which at the same time enables us to find how many different kinds of molecules are present and to determine the sedimentation constants of the various molecular species present in the solution, consists in measuring the velocity of sedimentation of the molecules in a very strong centrifugal field. The sedimentation constant reduced to water of 20°C. is given by the formula:

$$s_{20^\circ} = dx/dt \cdot 1/\omega^2 x \cdot \eta/\eta_0 \cdot \frac{(1 - V\rho_0)}{(1 - V\rho)} \quad (2)$$

where dx/dt = observed sedimentation velocity,

ω = angular velocity,

x = distance from center of rotation,

η = viscosity of solvent,

η_0 = viscosity of water at 20°C.,

V = partial specific volume of solute,

ρ = density of solvent, and

ρ_0 = density of water at 20°C.

By combining a determination of sedimentation equilibrium and of sedimentation velocity we are able to obtain a measure of the deviation of the molecules from the spherical shape (2). The ratio

$$\frac{M(1 - V\rho)}{6\pi\eta N \left(\frac{3MV}{4\pi N} \right)^{\frac{1}{2}}} \quad (3)$$

(where N is the Avogadro constant) ought to be unity if the molecules are spherical. A deviation from the spherical shape shows up as a value higher than unity for this ratio.

Certain complications are introduced if the sedimenting molecules are electrolytically dissociated (3). The sedimentation of the heavy part of the molecule is retarded because of the electrostatic attraction from the lighter ions. This effect may, however, be eliminated by the addition of a non-sedimenting electrolyte.

For the measurement of the sedimentation of molecules in centrifugal fields the following experimental problem has to be solved. A small column of liquid (height 4 to 12 mm., thickness 1 to 12 mm.) must be kept rotating at high speed for considerable time—during several hours in case of sedimentation velocity runs and during days or even weeks in the case of sedimentation equilibrium runs. The distance from the center of rotation should not be less than, say, 50 mm. because of the higher accuracy of measurement in homogeneous centrifugal fields. The temperature in the column of solution should be constant or changing but very slowly. The latter condition is of vital importance. An unfavorable temperature distribution within the rotating solution creates convection currents which completely vitiate quantitative measurements. For the same reason evaporation from the

surface of the liquid must be prevented. For sedimentation equilibrium measurements the height of the column of solution should not be more than 5 mm. because of the very long time required for the attainment of equilibrium in high columns. For sedimentation velocity determinations, on the other hand, the column should be as high as possible (not less than 10 mm.). The thickness of the layer of solution has to be chosen with regard to the concentration of the solution studied. Finally, the apparatus has to be built so as to permit of rapid and exact determinations of the concentration gradient in the solution while rotating at high speed.

The conditions just mentioned delimit the mechanical possibilities for the construction of the machinery (called ultracentrifuge) very much. For sedimentation equilibrium measurements on high molecular substances the centrifugal field need not exceed 10,000 times the force of gravity (corresponding to about 12,000 r.p.m. when the distance from the center of rotation is 50 mm.). In such cases where the concentration gradient can be measured by taking photographs within a wave-length region of high light absorption, it is even possible to determine molecular weights down to about 500 (4). On the other hand, by working at low speed (1500 r.p.m.) it is easy to measure molecular weights up to 5,000,000. The equilibrium method therefore allows us to master a large range with comparatively modest experimental means.

Figures 1 and 2 show the standard equipment now in use for equilibrium measurements. A small quantity of the solution to be studied (covered with oil in order to prevent evaporation) is enclosed in a sector-shaped cell (figure 1) provided with windows of crystalline quartz, and photographs of the concentration gradient set up by the rotation are taken during centrifuging, making

FIG. 1. ROTOR FOR SEDIMENTATION EQUILIBRIUM RUNS (CELLS AND SECTOR DIAPHRAGM REMOVED)

Centrifugal field 100 to 100,000 times gravity

FIG. 2. ULTRACENTRIFUGE FOR SEDIMENTATION EQUILIBRIUM RUNS

Speed 1000 to 12,000 r.p.m.

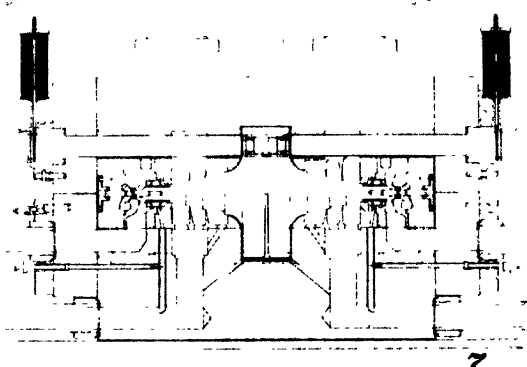
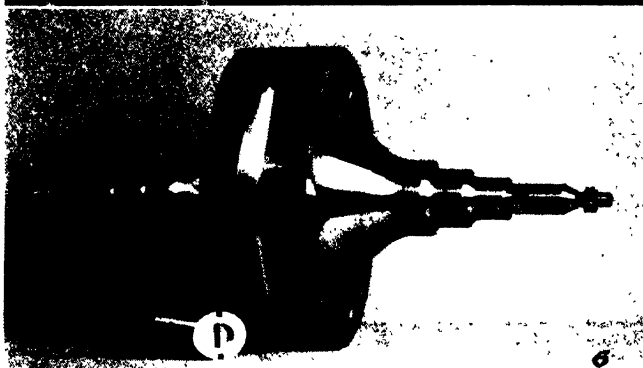
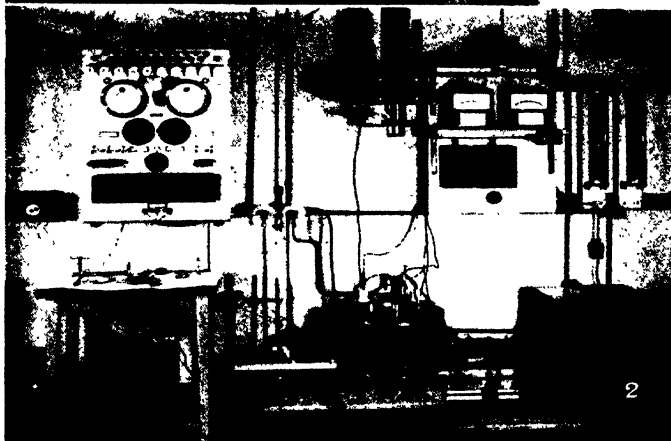
FIG. 3. OVALBUMIN IN A CENTRIFUGAL FIELD 5800 TIMES GRAVITY

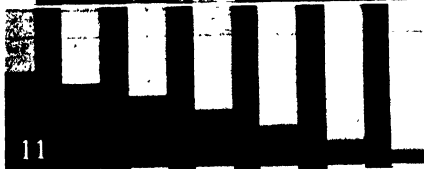
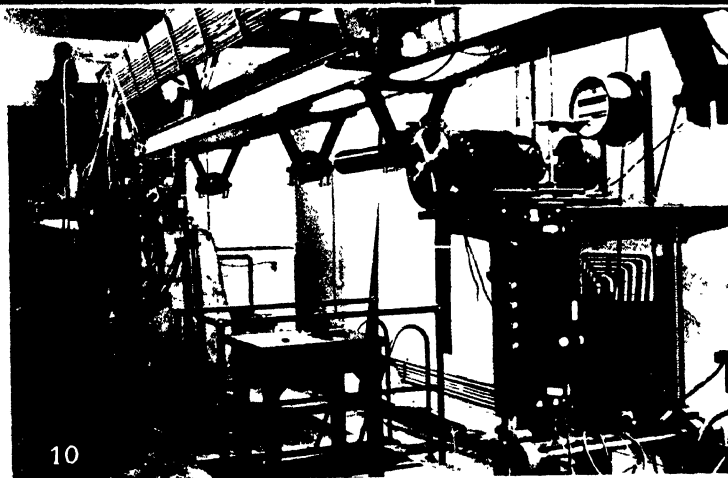
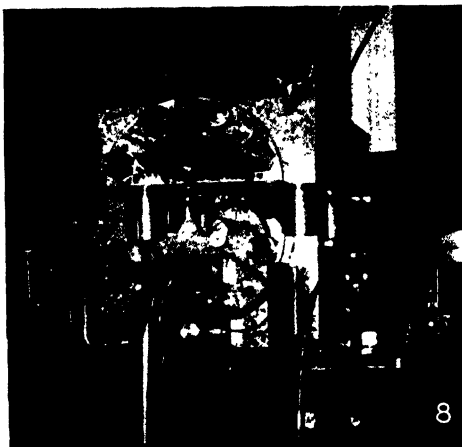
A, at the start; B, after sedimentation equilibrium has been reached. (J. B. Nichols.)

FIG. 6. ROTOR AND CELL FOR SEDIMENTATION VELOCITY RUNS

Centrifugal field 10,000 to 400,000 times gravity

FIG. 7. DIAGRAM OF OIL TURBINE ULTRACENTRIFUGE





use of the light absorption of the solute. The nickel steel rotor of 150 mm. diameter (figure 1) is supported upon a vertical shaft directly connected to the rotor of a special electric three-phase motor, the speed of which may be varied from 1000 to 12,000 r.p.m. by varying the frequency of the current feeding the stator. The centrifuge rotor as well as the rotor of the electric motor is surrounded by hydrogen at atmospheric pressure confined within a casing about the moving parts of the centrifuge. To further ensure constant temperature, the stator of the motor is water-cooled and the casing within which the centrifuge rotor moves is immersed in a water thermostat. Freedom from vibration is ensured by a special rubber support for the stator. Suitable arrangements for passing of a light beam through the centrifuge and for taking exposures are made.

Figure 2 gives a photographic view of the whole apparatus except the plate-holder part of the camera, which is placed in a room above the centrifuge. The water-cooled house for the mercury lamp can be seen to the right; then the light filters and the centrifuge follow from the right to the left. The horizontal illuminating beam is reflected vertically through the centrifuge by a quartz prism. Above the centrifuge is the photographic lens and part of the camera. On the wall are mounted the controlling instru-

FIG. 8. OIL TURBINE ULTRACENTRIFUGE

The lid is raised so as to show the rotor and the turbine and bearing chambers. Speed 10,000 to 75,000 r.p.m.

FIG. 9. ROTOR EXPLODED AT 58,000 R.P.M.

A, side view; B, end view

FIG. 10. OIL TURBINE ULTRACENTRIFUGE INSTALLATION

FIG. 11. SEDIMENTATION OF PHYCOERYTHRIN AT pH 4.7 IN A CENTRIFUGAL FIELD
260,000 TIMES GRAVITY (60,000 R.P.M.)

Time between exposures, 5 minutes. (K. O. Pedersen.)

FIG. 12. SEDIMENTATION OF OVALBUMIN AT pH 5.0 IN A CENTRIFUGAL FIELD
400,000 TIMES GRAVITY (73,500 R.P.M.)

Time between exposures, 5 minutes. (K. O. Pedersen.)

FIG. 14. SEDIMENTATION OF HELIX HEMOCYANIN AT THE ALKALINE STABILITY
BORDER pH 7.8

Centrifugal field 33,000 times gravity. Time between exposures, 5 minutes. The lowest boundary represents the heavy unchanged molecules; the middle and upper ones two different decomposition products. (K. O. Pedersen.)

FIG. 18. SEDIMENTATION OF τ -PHYCOCYAN AT pH 6.2

Centrifugal field 200,000 times gravity. Time between exposures, 5 minutes. The lower boundary represents molecules of weights 208,000, and the upper one molecules of weight $1/2 \times 208,000$. (Inga-Britta Eriksson.)

ments. Four aggregates of this type are at present mounted in the writer's laboratory. Figure 3 shows two photographs of the rotating column of an ovalbumin solution before and after sedimentation equilibrium has been reached (5), and figure 4 the same photographs registered by means of a microphotometer.

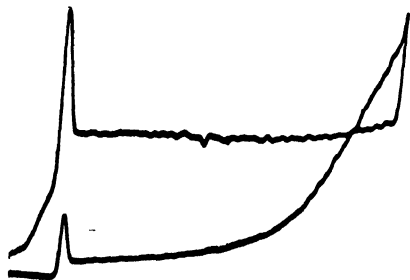


FIG. 4. MICROPHOTOMETER DIAGRAM OF THE TWO EXPOSURES OF OVALBUMIN OF FIGURE 3
(J. B. Nichols)

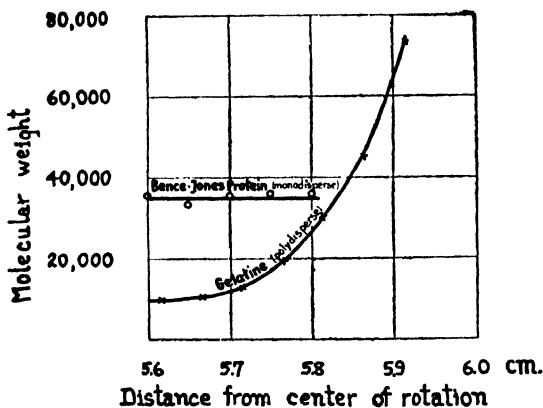


FIG. 5. RELATION BETWEEN MOLECULAR WEIGHT AND DISTANCE FROM CENTER OF ROTATION

Sedimentation equilibrium of Bence-Jones protein (monodisperse) and gelatin (polydisperse). (B. Sjögren and K. Krishnamurti.)

From this record and from a concentration scale photographed on the same plate, a curve giving the relation between solute concentration and distance from the center of rotation is constructed. The molecular weight is then calculated by means of equation 1. The diagram (figure 5) gives the values of the molecular weight as measured at different distances from the center of rotation in the

case of a homogeneous substance (Bence-Jones protein (6)) and an inhomogeneous substance (gelatin (7)).

A detailed molecular weight analysis requires the determination of sedimentation velocity in very strong centrifugal fields (from 30,000 times the force of gravity and upwards to several hundred thousand). Here we meet with great experimental difficulties. In order to gain sufficient separation of the different molecular species during the run, the height of the rotating column of solution should not be too small. We have chosen 12 mm. as standard height. The use of optical methods for measuring the changes in concentration during centrifuging makes it necessary to enclose the solution in a transparent cell. Two circular plates of crystalline quartz, 18 mm. in diameter and 10 mm. thick, define the column of solution in the direction of observation. Between the quartz plates is an elastolite plate with a sectorial aperture of 4° forming bottom and sides of the cell for the liquid. Around the quartz and elastolite plates is a collar of elastolite. This aggregate is introduced into a duraluminum collar (outer diameter 26 mm.) threaded at the ends and kept together by guard rings of the same material. Packings of very thin rubber membrane (0.06 mm.) are placed between the quartz plates and the elastolite plate. In order to delimit the light beam accurately, sector diaphragms of 2° are placed at the ends of the cell collar and fixed by means of two other guard rings. Cells of this construction withstand the action of centrifugal fields up to 400,000 times the force of gravity.

The rotor which carries the cell is shown in figure 6. It is made of chromium-nickel steel, is oval in shape (in order to lessen the strain), and has a diameter of 180 mm. across the cell holes. The thickness is 52 mm. at the periphery, and the weight 8.9 kg. The distance of the center of the cell holes from the axis of rotation is 65 mm. With a column of solution 12 mm. high the centrifugal force increases 20 per cent from top to bottom. When machining the rotor, two thin wings (total diameter 161 mm.) are left at right angles to the diameter bisecting the cell holes in order to prevent false light from reaching the photographic plate. Undue heating and temperature fluctuations are avoided by surrounding the rotor with a layer of hydrogen 1 mm. thick and of a pressure of about 25 mm. and outside of this with a heavy steel

casing. In this way the friction is reduced very much and a bath of good heat-conducting properties is created. The bearings of the rotor are lubricated and cooled by oil of 2 kg. per cm.² pressure. The driving agent is likewise oil acting on two small turbines (diameter 16 mm.), one on each end of the shaft of the rotor. By regulating the oil pressure from 1 to 16.5 kg. per cm.² the speed range 5000 to 80,000 r.p.m. can be covered. The rotor shown in figure 6 was tested at 78,000 r.p.m. and has been run regularly at 75,000 r.p.m., corresponding to a centrifugal field 400,000 times gravity at the center of the cell. Figure 7 gives an axial diagrammatic section through the ultracentrifuge with a previous type of rotor, and figure 8 gives a picture of it with the upper part of the heavy steel casing lifted, laying bare the rotor and the turbine chambers. The cell with its sector diaphragm is in vertical position upside down. Behind the centrifuge is the lamp house and the light filters. The two halves of the thick steel casing are held together by bolts of chromium-nickel steel firmly anchored in a concrete foundation. This arrangement has proved an efficient protection in case of accident. Explosion of the rotor has occurred twice, once from fatigue and another time because of flaw in the material. Pictures of the rotor and turbine chambers completely wrecked by such an explosion are shown in figure 9. Figure 10 gives a total view of the installation showing, from right to left, the stroboscope for measuring the speed, the camera, the centrifuge on its foundation, and the coolers. The compressor for delivery of pressure oil, together with oil filters and vacuum pump, is mounted in a lower room, the entrance to which is seen in the middle of the picture. The switchboard with all the control instruments, such as voltmeters, ammeters, manometers, vacuum meters, resistance thermometers, thermocouples, etc., is to the left of the big room and is not shown in the picture. Two high-speed ultracentrifuge aggregates of this rather costly type are now available in the writer's laboratory, thanks to the generosity of the Rockefeller Foundation and the Nobel Foundation.

As an example of the determination of sedimentation velocity, a series of pictures of *r*-phycoerythrin ($M = 208,000$), the red protein of the algae, sedimenting in a centrifugal field 260,000 times the force of gravity (speed 60,000 r.p.m.) is given in figure 11. The time interval was only five minutes. The boundary be-

tween solution and pure solvent is very sharp, demonstrating the high degree of molecular homogeneity of this protein. In the last exposures it has become slightly blurred, owing to diffusion. Figure 12 shows the sedimentation pictures (time interval, 10

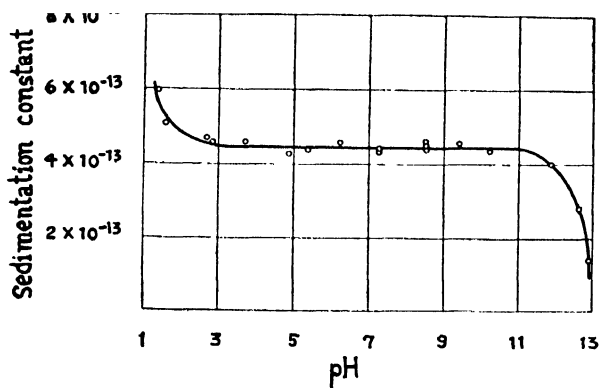


FIG. 13. pH STABILITY CURVE OF OVALBUMIN
(B. Sjögren)

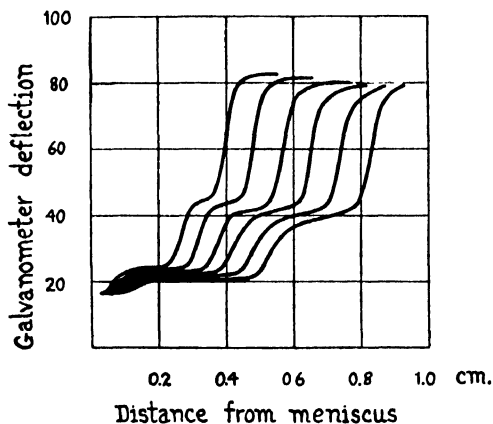


FIG. 15. SEDIMENTATION CURVES TRACED FROM THE MICROPHOTOMETRIC RECORDS OF THE EXPOSURES OF FIGURE 14
(K. O. Pedersen)

minutes) from a run with ovalbumin at 400,000 times gravity (speed 73,500 r.p.m.)

By means of measurements of molecular sedimentation in centrifugal fields a detailed study of the properties of protein solu-

tions has been carried out in the writer's laboratory (8). Some of the main results may be mentioned.

Most of the native proteins have been found homogeneous with regard to molecular weight (monodisperse). By changing the pH of the solution within certain limits the molecular weight remains unchanged. Each protein has a characteristic pH stability region. When the borders of the stability range are exceeded, disintegration or aggregation takes place. Figure 13 shows the pH stability curve for ovalbumin (9) ($M = 34,500$). The rapid fall in the sedimentation constant at pH 12 shows that disintegration

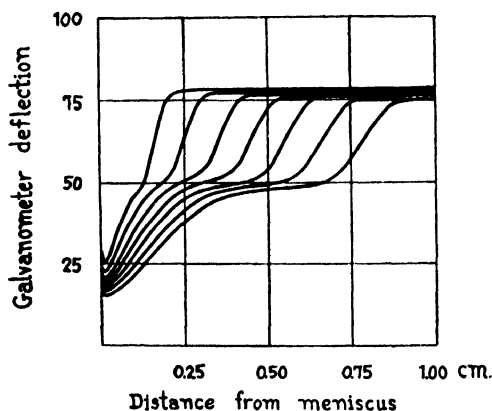


FIG. 16. SEDIMENTATION CURVES OF AMANDIN AT THE ALKALINE STABILITY BORDER pH 12.2

Centrifugal field 100,000 times gravity. Time between exposures, 5 minutes (last curve 2 hours after start). Forty per cent of the substance is dissociated in $1/6$ molecules of weight 34,500 (lower part of curves), and 60 per cent is unchanged with the weight 208,000 (upper part of curves). (B. Sjögren.)

occurs in the neighborhood of this pH, while the rise in acid solutions points to aggregation.

The molecular weight analysis by means of the ultracentrifuge has in several cases demonstrated the existence of one or two decomposition products of well-defined molecular weight, together with unchanged molecules at the pH stability border. A beautiful example of this phenomenon is shown by the hemocyanin of the Helix-blood. Figure 14 gives the sedimentation pictures and figure 15 the microphotometric records from an ultracentrifugal run at pH 7.8 (unpublished determinations by K. O. Pedersen). The lowest boundary lines in figure 14 and the highest parts of

the curves in figure 15 represent the unchanged hemocyanin molecules ($M = 5,000,000$), while the two upper boundaries are caused by two decomposition products $1/2$ and $1/16$ th of the original molecule. It is of interest to note that hemocyanins of these two types have been found as quite stable and normal constituents of the blood of certain crustaceans (10).

A similar diagram for amandin (11) at pH 12 is shown in figure 16. The unchanged amandin molecules possess the weight 208,000, while the decomposition product has a weight of about 34,500 or $1/6$ th of the original molecule. It seems therefore that the amandin molecule is dissociated into six parts, each of them of the same weight as the molecule of egg albumin.

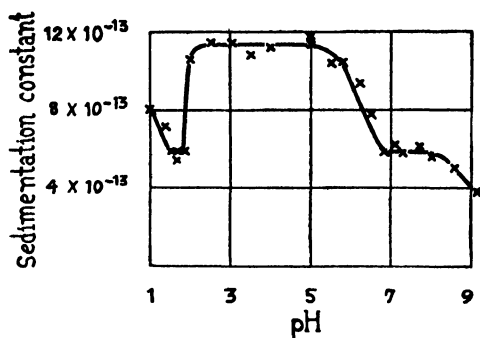


FIG. 17. pH STABILITY CURVE OF *r*-PHYCOCYAN
(Inga-Britta Eriksson)

Other examples of dissociation of the molecule into a few well-defined parts when exceeding a certain pH value are to be found among the algae proteins. The phycocyan of the blue-green algae ($M = 208,000$) is at a pH of 6.8 decomposed to about 35 per cent in half molecules (12). The phycocyan from the red algae (13) has a very peculiar stability curve figure 17. Within the middle range, pH 2.5–5.0, the molecular weight is 208,000. On both sides are two regions, pH 1.5–1.8 and pH 6.8–8.0, within which complete dissociation in half molecules occurs. On the borders between the regions for whole and half molecules the sedimentation constant, when measured in centrifugal fields of medium strength, seems to change rapidly with pH. If such a solution is exposed to the action of a very strong field, however, we find that it is a mixture of whole and half molecules. Figure 18

gives the sedimentation pictures showing the two boundaries and figure 19 the microphotometric record of exposure No. 5. Outside the two regions of half molecules there occurs aggregation in the acid direction and decomposition in the alkaline direction.

The dissociation of phycocyan in half molecules when exceeding certain pH values is connected with a general relationship concerning the molecular weights of the proteins. We have found that the molecules of most of the homogeneous native proteins are simple multiples or submultiples of 34,500, which is the molecular weight of ovalbumin. Only a very limited number of different molecular weights are represented among the proteins. On

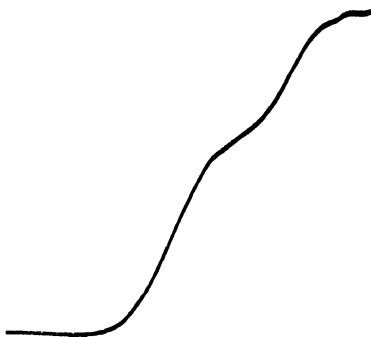


FIG. 19. MICROPHOTOMETRIC RECORD OF EXPOSURE NO. 5, FIGURE 18

Showing the sedimentation of whole and half molecules in a solution of *r*-phycocyan at pH 6.2. (Inga-Britta Eriksson.)

the other hand, we know a large number of proteins differing widely with regard to chemical composition, isoelectric point, and light absorption. This means that chemically different proteins may have the same (or nearly the same) molecular weight. As a matter of fact we find that the numerous proteins fit into a few molecular weight classes. Recent investigations have shown that this regularity probably obtains from the lowest molecular weight so far observed for a protein, or 17,000, up to the highest weight, or 5,000,000. It seems that just about a dozen different steps are required in order to proceed from the lowest to the highest weight. With increasing weight the absolute interval between the steps becomes larger and larger. Thus there are six different

molecular weights between 17,000 and 200,000, and also six between 300,000 and 5,000,000.

What reality—chemical or physiological—is the explanation of this puzzling display of figures we do not know as yet. But we may hope that a continued study of the native proteins by means of the ultracentrifugal methods outlined above will help us to solve this riddle.

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THE CHEMISTRY OF VITAMINS A AND C¹

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Received November 8, 1933

Absence or insufficiency of vitamins in the daily food ration will cause certain well-defined symptoms of diseases. To these biological effects we really owe the discovery of the vitamins; they were also absolutely essential for their purification and final isolation. Eight or nine vitamins are known today, and only four of these have been prepared in a pure, or at least nearly pure, state. These are vitamin A, the fat-soluble factor of growth; B₁, the antineuritic vitamin; C, the antiscorbutic vitamin; and D, the antirachitic vitamin. Only for vitamins A and C can structural formulas be advanced. These two have also been a principal subject of our own investigations, and therefore, I shall devote myself mainly to them in this lecture.

I begin with the antiscorbutic factor, vitamin C. Zilva several years ago showed that highly purified vitamin C preparations were free from nitrogen, and that the antiscorbutic factor must have a molecular weight like a hexose. At about the same time C. G. King greatly improved the methods for concentrating vitamin C in lemon juice, and Tillmans made the important observation that the reducing power of many plant juices towards iodine and other weak reductive agents, like dichloroindophenol, in acid solution, is in proportion to the antiscorbutic efficiency of these plant juices. From this parallelism he concluded that vitamin C itself must be a powerfully reducing substance.

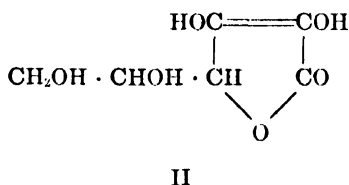
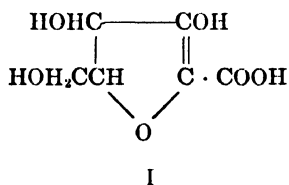
About five years ago Szent-Györgyi isolated from the cortex of the adrenal gland and later on also from plants, a well crystallizing substance, having the empirical formula C₆H₈O₆. In acid solution it showed strong reducing power against iodine and similar

¹ Presented at the Joint Session of the Biochemical, Medical, and Organic Divisions at the Eighty-sixth Meeting of the American Chemical Society in Chicago, September 14, 1933.

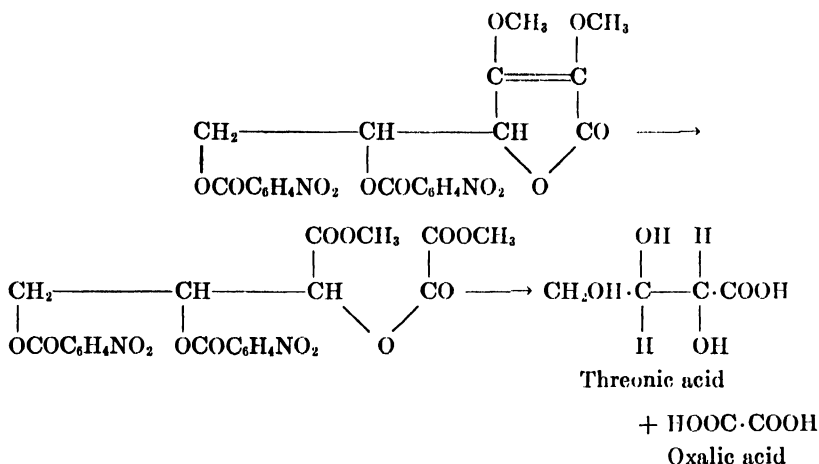
oxidative substances. In 1932 C. G. King isolated the identical substance from lemon juice and discovered that it cured animals suffering from scurvy. Simultaneously, after Tillmans' investigations in regard to the reducing properties of the antiscorbutic factor had become widely known, Szent-Györgyi tested his substance for antiscorbutic properties and found that it had a curative effect on guinea pigs in doses of 0.5–1 mg. per day. To this substance the name ascorbic acid was afterwards given. Zilva, Dalmer and Moll, Tillmans, von Euler, and others confirmed its efficiency in healing scurvy.

We fractionated by recrystallization 25 g. of ascorbic acid, until the last fraction, the least soluble one, amounted to about 1 g. We tested every fraction for its reducing power against iodine. No differences could be detected. According to von Euler and Demole the antiscorbutic efficiency of all fractions was also identical. There is therefore hardly any doubt about the homogeneity of this substance.

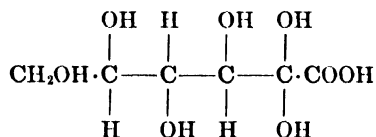
The constitution of ascorbic acid has been the subject of a number of investigations. I mention Szent-Györgyi with his coworker Vargha, Haworth, Hirst, Smith and Reynolds, Micheel, and finally also our own institute in Zürich. It is certain that ascorbic acid is a monobasic acid, with four hydroxyls in all. Two of them are enolic and account for the acid character, and two are alcoholic hydroxyls, of which one is primary, giving a triphenylmethyl ether. The other alcoholic hydroxyl must be in either the 2- or the 3-position to the first one, as ascorbic acid forms with acetone a well crystallizing acetone compound; this reaction is characteristic for 1,2- or 1,3-glycols. Micheel oxidized the dinitrobenzoic acid ester of the enolic methyl ether of ascorbic acid and found among the products of degradation *l*-threonic acid and oxalic acid. This result would give to either one of the two following formulas a high degree of probability.



According to I, ascorbic acid would be a furan derivative, according to II, a γ -lactone (Hirst, v. Euler). If we assume the lactone structure the degradation would proceed as follows:



At present the lactone structure seems to be the more likely one. Dimethylascorbic acid yields with alcoholic ammonia a derivative containing nitrogen, and the two methoxyl groups are still intact. It can be regarded as an amide resulting from the γ -lactone through an opening of the lactone ring. The formation of idonic acid

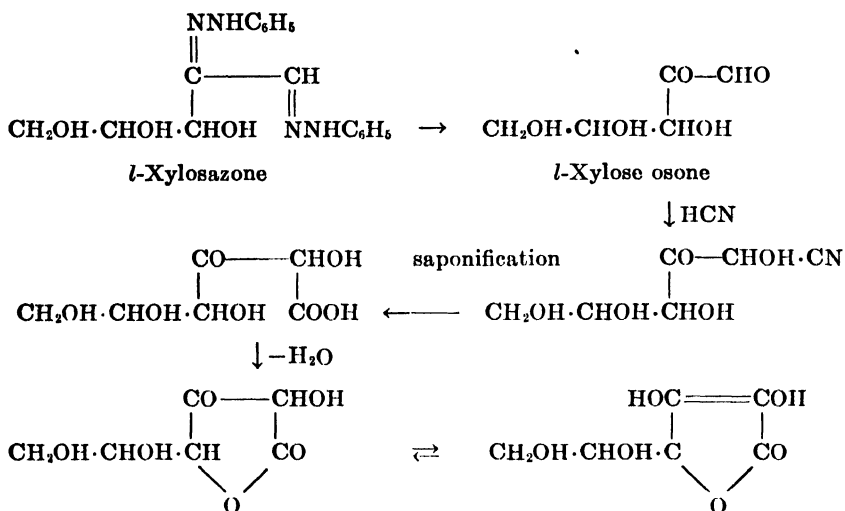


by catalytical reduction of ascorbic acid also speaks in favor of this lactone structure.

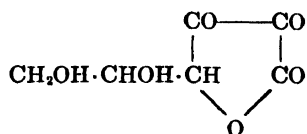
That the lactone structure is the correct one, we could recently prove in the following manner: Dimethylascorbic acid reacts with Grignard reagent without splitting off a methoxyl group. This is only possible if ascorbic acid is a lactone, as a methyl ester would react by removing of one mole of methyl alcohol.

Reichstein in Zürich has succeeded in preparing ascorbic acid by synthesis. The synthesis would be in good agreement with the lactone structure, II, or at least one very closely related to it. It would however not exclude the furan structure I. Starting from

l-xylose, Reichstein prepared first the osazone and from this the osone. Treatment of the osone with hydrocyanic acid gave a nitrile, and the saponification of the latter yielded ascorbic acid. The yield was about 20 per cent figured on the osone. Chemical and physical properties are absolutely identical with those of ascorbic acid. The vitamin C efficiency is now being tested.



The most characteristic chemical property of vitamin C is its extraordinary power of reduction. In acid solution it uses an amount of oxygen corresponding to the oxidation of two hydrogen atoms. The product of this oxidation, the dehydroascorbic acid, can easily be reduced again to its mother substance, for instance, by means of sulphuretted hydrogen. The dehydro acid was isolated by us in pure, but amorphous form. The analysis shows that it has two hydrogen atoms less than ascorbic acid, and the determination of the free hydroxyls, according to Zerewitinoff, gives only two hydroxyls. This result can only be explained by assuming that the oxidation has removed the hydrogen from two of the hydroxyl groups, most likely forming a diketone of the constitution:



Dehydroascorbic acid has not lost its antiscorbutic efficiency; in fact, it shows about the same activity as ascorbic acid itself.

For guinea pigs afflicted with scurvy, the healing dose of vitamin C is at least 0.5 mg. per day. This dose is about 100,000 times as large as the curative dose of vitamin D, and 10,000 times the amount needed of vitamin A. There is of course the possibility that ascorbic acid is not the vitamin itself, but that it acts as provitamin, from which the organism only creates the C-factor. However there is really at present no basis for this hypothesis.

Pure ascorbic acid has now become an easily accessible vitamin, obtainable in any desired amount. This will undoubtedly give rise to important researches, physiological as well as biochemical. I am quite sure that very interesting new functions of this vitamin will yet be discovered. We have already observed that ascorbic acid acts as activator of the catheptic proteoses. Catheptic proteolytic ferments, which have lost their natural activators and have become inactive, can be reactivated with ascorbic acid. In this respect vitamin C resembles cystein and glutathione, two substances which, according to Waldschmidt-Leitz, also undergo reversible oxidation. This coferment effect depends perhaps on the oxido-reductive potential.

I now proceed to my next subject, vitamin A. This is one of several vitamins necessary for the proper growth of the animal. It therefore is called the fat-soluble growth factor. However, deficiency of vitamin A not only produces loss in weight, but also hemeralopia, xerophthalmia, degeneration of nerve fibers, skin diseases, and affections of the mucous membrane, etc.

The history of vitamin A is still young, but has nevertheless been full of interesting episodes. Osborne and Mendel, McCollum and Davis were the first who ascertained the presence of factor A in cod-liver oil and butter. Hopkins found that cod-liver oil loses its curative qualities if air is bubbled through it. Then came Steenbock and his school with their thorough and important investigations. They examined numerous plants and their extracts, also food stuffs, as to their vitamin A content. They brought out the interesting fact that only such vegetable and similar products had a vitamin A effect, as were rich in certain yellow pigments, the so-called carotenoids. From this they concluded that vitamin A must stand in some relation to these pig-

ments. Steenbock tested carotene for vitamin A effect, and claimed that it had curative properties. Drummond repeated these tests, and found that it was ineffective. He drew the conclusion that Steenbock's positive results must have been due to some foreign substance accompanying the carotene, and for years this remained the generally accepted opinion.

In 1927 von Euler was able to harmonize these contradictory statements. Drummond had used a vitamin A-free diet plus carotene. von Euler's investigations established the important fact that the above ration had indeed no vitamin A curative effect. The cause of this, however, was not inefficiency of carotene, but the fact that this ration was not only devoid of vitamin A, but also of vitamin D. Vitamin A however can only exert its curative powers in presence of vitamin D and the other vitamins. von Euler therefore added carotene and vitamin D to the ration used by Drummond and now the curative effects were the same as of good cod-liver oil, which as you know is rich in both of these vitamins.

These new facts, however, were not generally accepted. It was argued that cod-liver oil, a rich source of vitamin A, does not contain any carotene, but some other substance with an absorption spectrum totally different from that of carotene. Th. Moore finally solved the riddle. The liver is the storage house for vitamin A. Moore found that the vitamin A content of the liver decreases rapidly and finally disappears completely, if animals are kept on a vitamin A-free diet. After an addition of carotene to the diet, the vitamin A content of the liver increases again rapidly. The explanation is, that carotene is a provitamin of the A factor which means that it is transformed by the organism into the vitamin.

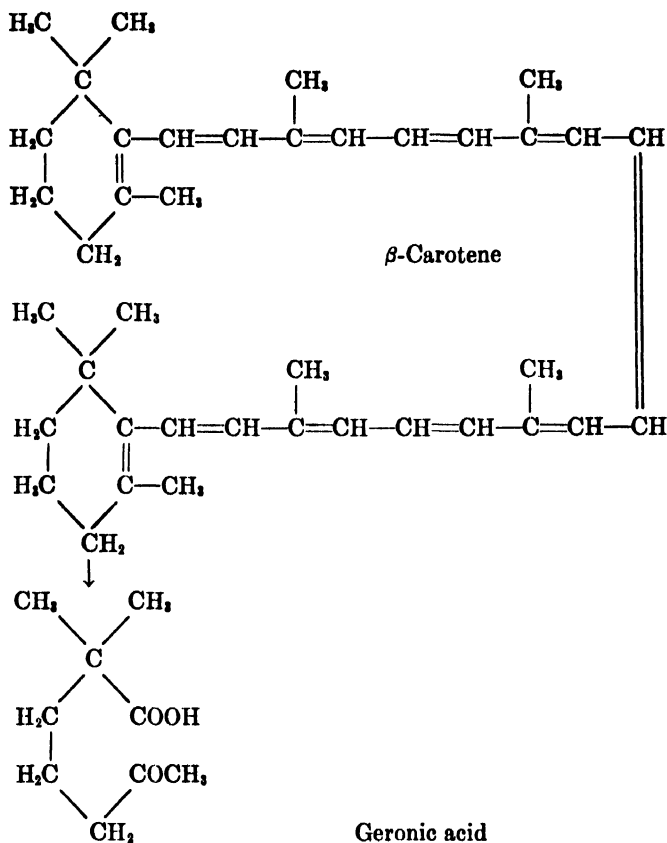
von Euler and our own investigations have shown that of all naturally occurring carotenoids, only the carotenes have this provitamin A effect. Vegetable carotene is hardly ever homogeneous. It is a mixture of two or more isomeric forms, known as α -, β -, γ -, and possibly even still another one. The γ -carotene of Kuhn is present only in traces; β -carotene is always the main component and can perhaps occur without any of the others. The amount of the α -carotene varies greatly, from traces to 20 or more

per cent. The separation of these various isomeric carotenes from each other was a tedious and not very satisfactory process. Fractionation by crystallization, adsorption on specially prepared aluminum hydroxide or Fuller's earth, give a certain degree of purification and enrichment of one of the components. To get a complete separation, the process must however be repeated over and over again. In search of better adsorbents we recently found that calcium hydroxide or calcium monoxide are greatly superior. The process is carried out like a chromatographic analysis. One adsorption suffices to bring about a clean separation of α -carotene from β -carotene, and α -carotene is now a readily accessible substance. α -, β -, and γ -carotene have slightly different melting points and solubilities. Their absorption spectra also show different lines. Only α -carotene is optically active. (See table 1).

TABLE 1

	MELTING POINT	MAXIMA OF ABSORPTION (CS ₂)	$[\alpha]_{544}$
	<i>degrees C.</i>	$\mu\mu$	
α -Carotene, C ₄₀ H ₅₆	183	509, 477, 448	+323°
β -Carotene, C ₄₀ H ₅₆	183	520, 485, 450	Inactive
γ -Carotene, C ₄₀ H ₅₆	174	533, 496, 463	Inactive

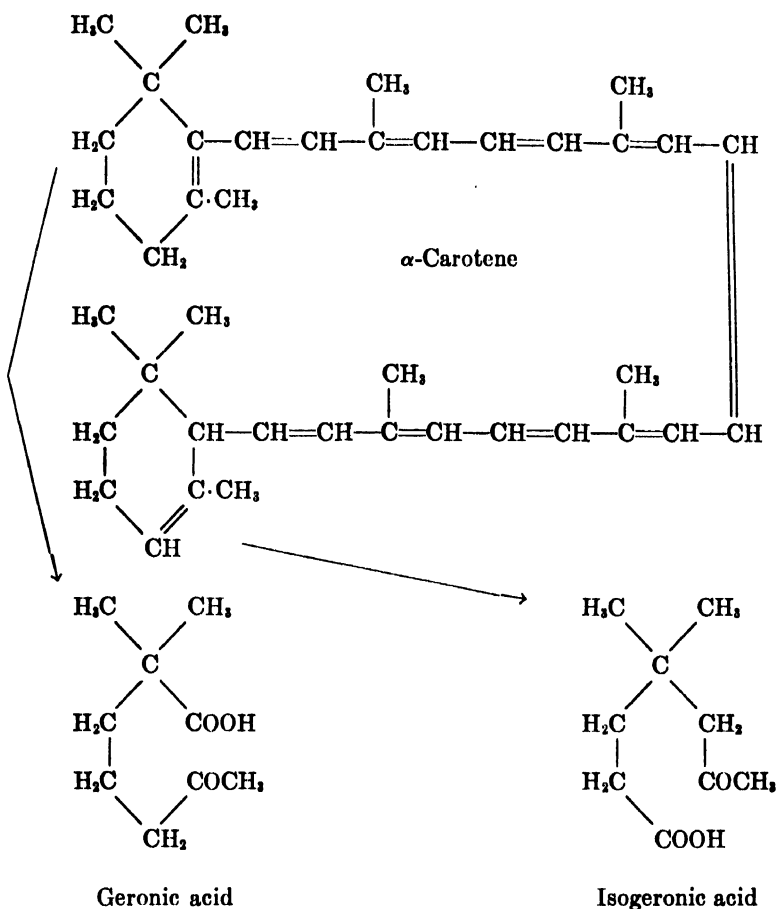
The determination of the constitution of these carotenes and especially of the most important one, β -carotene, has been the subject of long investigations at our Zürich institute. Today the structural formula has been definitely proven. β -carotene, C₄₀H₅₆, is an unsaturated hydrocarbon, containing eleven double linkages. Through catalytic reduction it takes up eleven moles of hydrogen. Degradation by oxidation has been particularly useful for elucidating the chemical structure. Ozonization gave geronic acid, permitting the conclusion that the carotene molecule must contain carbon rings like β -ionone. Comparing the yields of geronic acid obtained by ozonization of β -ionone and β -carotene, we came to the conclusion that the carotene molecule must contain two β -ionone rings as expressed by the following formula:



Degradation of β -carotene with potassium permanganate gives four moles of acetic acid; with chromic acid six moles. This proves six methyl groups in the molecule. Four of these, those which give acetic acid already with permanganate, belong to the aliphatic chain.

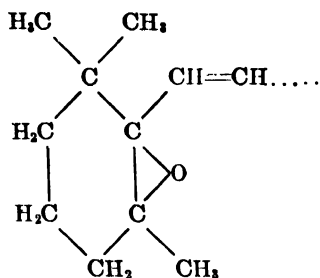
Time is too short to give all the reasons for this formula for β -carotene. It suffices to say, that it is so far in excellent agreement with all experimental data.

α - and β -carotene are isomeric, and their isomerism is due to the different position of the double linkages. Ozonization of α -carotene yields geronic acid, and in contrast to β -carotene also isogeronic acid. The only formula which fully explains these results is the following:



The asymmetric C atom in α -carotene accounts for the optical activity of this substance.

α -, β - and γ -carotene are not the only provitamins of the A factor. They are the only ones, as far as we know, occurring in nature. Four carotene derivatives however have been prepared, which can act as provitamins. The first of these is carotene iodide, a well crystallizing substance. Another one is the dihydrocarotene, which is a product of partial catalytic reduction and probably not a homogeneous substance. The third is a monohydroxy carotene, and the last an oxide of carotene, whose oxygen atom is most likely in the form of an inner ether.



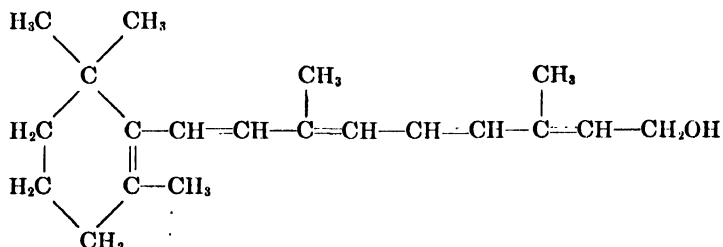
In all four of these derivatives, at least one of the original two β -ionone rings is still unchanged. If both of these rings are altered, as is the case in the xanthophylls or phytoxanthins, through substitution of hydrogen atoms by hydroxyl groups, the ability to act as provitamins disappears completely. The presence of at least one β -ionone ring is therefore absolutely essential for the vitamin A effect. This fact is no longer surprising, since we know the close relationship between β -carotene and vitamin A.

Liver oils from various animal sources differ greatly in their vitamin A content. Not only does the amount vary between the different species, but it is also greatly influenced by their food. If the food is rich in carotene, the vitamin A, which is stored in the liver, increases enormously and far above the normal amount. Fish-liver oils are much richer in vitamin A in summer than in winter: for instance, halibut liver oil contains twenty times more in summer. According to von Euler's and our own investigations the liver oils from *Hippoglossus hippoglossus*, *Scombrosox saurus*, *Rhombus maximus* and of the Japanese fish, *Stereolepis ishinagi*, contain from 200 to 2000 times as much vitamin A as common cod-liver oil. The discovery of this fact was of great importance. Without it we would hardly have been able to carry on our investigations.

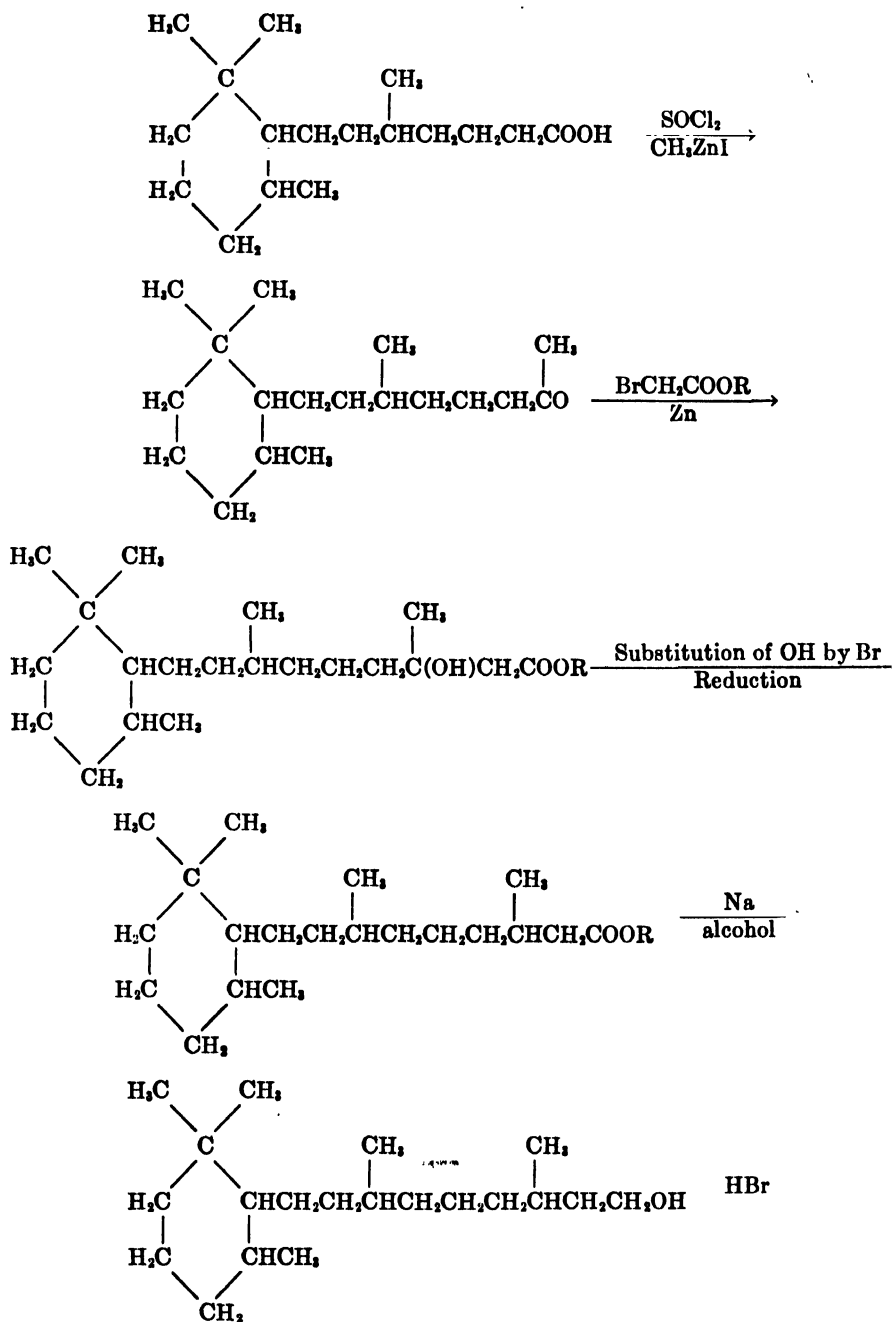
Fractionation; the removal of foreign substances by freezing out at very low temperatures, and methods of adsorption led finally to vitamin A preparations with constant analytical data. These preparations could at least be regarded as highly concentrated forms of vitamin A.

This period of my work will always remain fixed in my memory as one of the most fascinating of my laboratory experiences. Up to the time when we started using those liver oils, very rich in

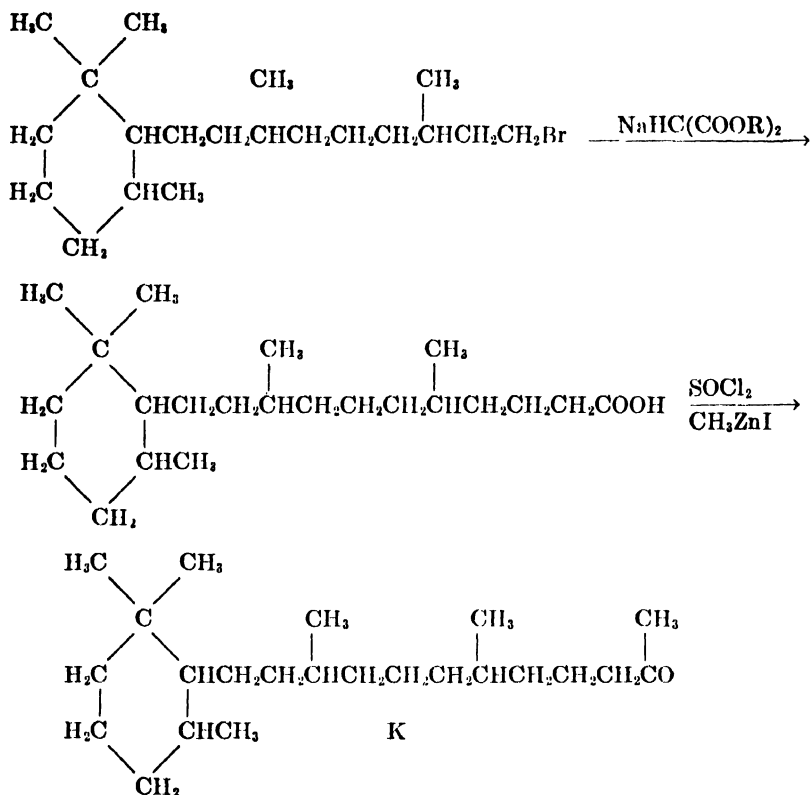
vitamin A, we had of course experimented only with the unsaponifiable residue from cod-liver oil. Tedious processes of purification and concentration gave us products with as high as 400 C.L.O. units, the usual standard for measuring the vitamin A content. You can well imagine what it meant to us, when we found oils where this unsaponifiable residue, without any further purification, showed already C.L.O. units as high as 200 to 800. Methyl alcoholic solutions of these crude residues were purified by freezing out the sterines and other foreign substances at low temperatures. The C.L.O. unit rose promptly to 5000. A repetition of this process at 70°C. below freezing gave a product with 8000 C.L.O. units. Fractional adsorption on fibrous aluminum hydroxide gave a further rise to 9000, and a second adsorption finally even to about 10,000 C.L.O. units. Then it stopped, and renewed adsorptions on aluminum hydroxide did not give any further improvement. Quite recently we found in calcium hydroxide a much better and especially more selective adsorbent. Through adsorption on calcium hydroxide a small amount of a foreign substance with a distinctly different absorption spectrum can be removed. The analytical data of the main fraction, however, remain unchanged. The final product is a very viscous light yellow oil. It can be distilled without decomposition under very much reduced pressure, boiling at a temperature of 137–138°C. Our investigations resulted in the following formula for vitamin A.



The degradation of vitamin A by oxidation is most illuminating and of great importance. Just like β -carotene, it gives geronic acid and three moles of acetic acid. Esterification establishes one alcoholic hydroxyl group. Catalytic reduction indicates five double linkages. Quite recently we synthesized the perhydro-vitamin A and now the structural formula has become a certainty.



Perhydro-vitamin A



A comparison of the formulas of β -carotene and vitamin A clearly reveals their structural and genetical relationship. The β -carotene molecule is split in half and one alcoholic hydroxyl appears at the end of the open chain.

Scientists of many nations have harmoniously worked together in the new field of vitamins. Americans and American institutions, however, can claim the honor of having been the real pioneers. They were the first to tackle this most difficult and unpromising problem. They used strictly chemical and physiological methods for the isolation and identification of these, at that time nearly mythical, substances. To them science owes a great debt of thanks. For me it has therefore been a special pleasure and a still greater honor that I should have been permitted to deliver this lecture before your Society. I want to express to you my sincerest thanks and appreciation.

THE COMBUSTION OF CARBON

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The rate of combustion of carbon under ordinary conditions is determined, not by the speed of the chemical reaction of oxygen and carbon, but by the rate at which oxygen can diffuse from the ambient atmosphere to the fuel surface. The rate of the primary surface reaction can be determined only under such conditions that the limiting effect of the diffusion process is removed. Such conditions are described in the first part of this paper in the discussion of experiments on combustion in oxygen at low pressures. The speed of the diffusion process itself may be determined from the measurements, described in the second part of the paper, of rates of combustion at ordinary furnace temperatures and pressures. The third part is a discussion of mathematical analyses of the entire process, in an attempt to express the rate of the reaction in terms of known physical quantities. It is to be noted that this paper does not consider two preliminary processes—the heating of the fuel and the expulsion of its volatile portion—which occur in industrial furnaces.

I. EXPERIMENTS AT REDUCED PRESSURES

In order to determine the nature of the primary reaction between gaseous oxygen and a carbon surface, a succession of oxygen molecules should be permitted to impinge just once on a clean carbon surface, and the products should be removed from the sphere of reaction as soon as they are liberated. This ideal may be approached by the use of high vacuum technique.

In 1915 Langmuir (17) reported experiments on the oxidation of electrically heated carbon filaments suspended in evacuated bulbs cooled by liquid air. Provision was made for admitting gases to the bulb and for measuring the gas pressure by means of a McLeod gauge. With the filament at 950°C., carbon dioxide was the only product of combustion by oxygen, but as the temperature was increased, increasing amounts of carbon monoxide were formed. In order to recover all the oxygen, even as oxides of carbon, it was necessary to heat the filament to 2200°C. for half an hour, pumping continuously. When carbon dioxide was admitted to a filament at about 930°C., carbon monoxide was formed at the same rate at which

carbon dioxide disappeared. Evidently half of the oxygen remained in or on the carbon, in agreement with recent work of Broom and Travers (2).

Additional evidence that oxygen is very strongly held by clean carbon surfaces was supplied by sorption measurements on charcoal (18, 21). Only a small part of the oxygen admitted at room temperature can be removed by evacuation alone; it is necessary to raise the temperature while evacuating, when the oxygen comes off as oxides of carbon. The strength of the binding is indicated by measurements of the heat evolved in sorption (11, 14) which, for the first few increments of oxygen added, may be greater than the heat of combustion of carbon.

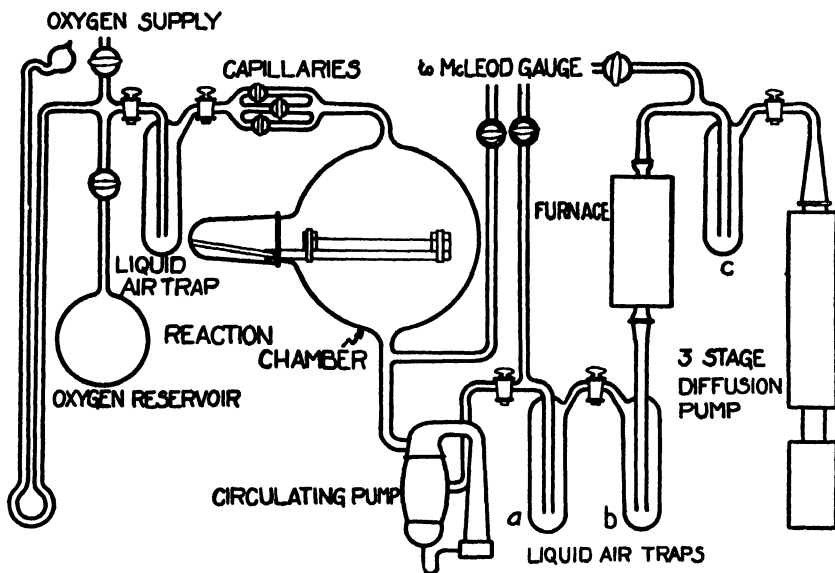


FIG. 1. DIAGRAMMATIC LAYOUT OF APPARATUS FOR LOW PRESSURE COMBUSTION OF CARBON

Quantitative measurements of the rate of combustion of graphite at oxygen pressures of the order of 10^{-3} mm. of mercury were attempted by V. Sihvonen (27), using apparatus similar to Langmuir's but in which only a condenser tube sealed to the bulb was cooled with liquid air. The graphite sample was of measured size, and the reaction bulb contained a loop of platinum wire on which the carbon monoxide could be burned at the end of each run. Experiments were made with both flowing and static gaseous atmospheres, but both Sihvonen and Eucken, who also presented a discussion of the data (8), base their conclusions on the runs made with stationary atmospheres, although in this case secondary reaction is only partially prevented because of the presence in the atmosphere of a finite

concentration of carbon monoxide. Apparently because the technique was not sufficiently refined, the results of these experiments are not very consistent, but they agree in order of magnitude with those found later by L. Meyer (22), whose results show more clearly the relations among the variables.

Meyer reported results obtained in the apparatus shown diagrammatically in figure 1, in which oxygen at low pressures was passed at high velocity over the surface of electrically heated carbon filaments suspended between graphite blocks. The products of combustion were removed from the

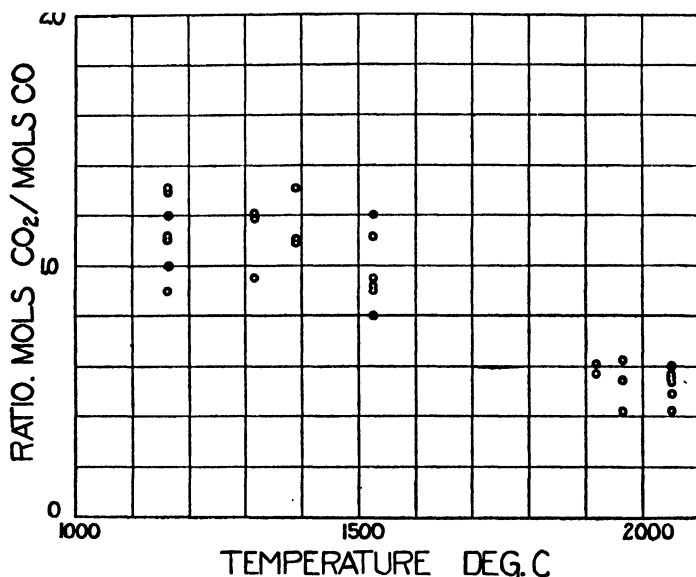


FIG. 2. LOW PRESSURE COMBUSTION OF CARBON

Ratio of carbon dioxide to carbon monoxide in products of reaction at various temperatures.

reaction chamber by a mercury diffusion pump, carbon dioxide was frozen out in the liquid air trap *a*, carbon monoxide was oxidized in a furnace containing palladized asbestos and removed from the gas stream by freezing in the traps *b* and *c*, and the remaining oxygen pumped out of the system by the three-stage mercury diffusion pump.

The pressure in the reaction chamber was about 10^{-3} mm. of mercury, which allowed oxygen molecules a free path of the order of magnitude of the bulb diameter, while the high velocity permitted an average time in the reaction chamber long enough for about a hundred collisions. From these and other data the probable error due to secondary reaction was

estimated to be about 15 per cent. The method of gas analysis was found by blank runs to have an average error of about 7 per cent.

In the first runs ordinary carbon lamp filaments were used, but reproducible results could not be obtained unless they were built up by flashing them for 1 to 2 minutes at 2500°C. in an atmosphere of 1/3 methane and 2/3 hydrogen, thus producing uniform surfaces of graphite whose basal planes were found, by x-ray analysis, to be parallel to the filament axis. The treated filaments had the physical characteristics of exceptionally

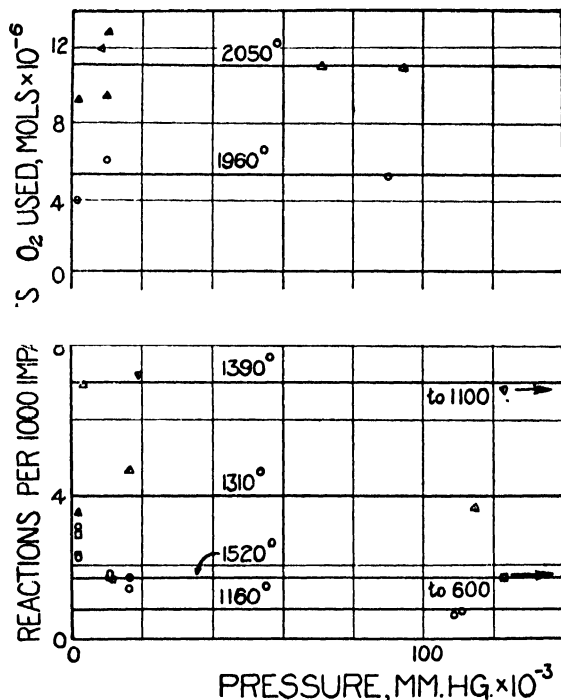


FIG. 3. LOW PRESSURE COMBUSTION OF CARBON

Rate of the reaction at various pressures in two temperature ranges. Numbers on lines indicate temperatures in degrees C.

pure samples of graphite, and could be used for three or four runs before pitting due to the combustion reaction made them useless.

The results of the experiments are given in figure 2, in which the ratio of the two products of reaction is plotted against temperature, and in figure 3, in which the rate of use of oxygen is plotted against pressure. It will be noticed that the results fall into two temperature groups, with a transition between 1450°C. and 1650°C. In the low temperature group, the ratio CO_2/CO is approximately constant within the limits of ex-

perimental error at about 1, as shown by figure 2, while, as is shown by the lower part of figure 3, in this temperature range the rate of reaction is proportional to the number of impingements of molecules on the carbon surface, i.e., to the gas pressure. The temperature coefficient of this reaction corresponds to an energy of activation of 20 to 30 kilocalories. In the higher temperature range, the ratio CO_2/CO is only about 0.5, while the rate of use of oxygen, plotted in the upper part of figure 3, is independent of the pressure.

Sorption measurements throughout the temperature range indicated that appreciable sorption occurred only in the low temperature region, where the amount of oxygen sorbed at any temperature was proportional

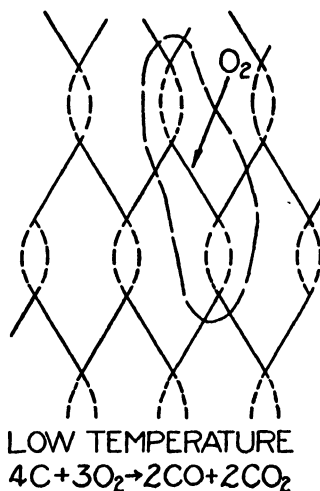
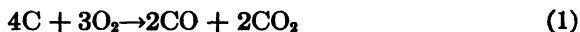


FIG. 4. MECHANISM OF COMBUSTION ACCORDING TO L. MEYER

Apices of hexagons represent carbon atoms; dotted lines represent adsorbed oxygen atoms; O_2 with arrow represents oxygen molecule impinging from gas phase, when section within dashed lines breaks away from solid phase forming $2\text{CO} + 2\text{CO}_2$.

to the pressure, and the amount sorbed at any pressure fell off with increasing temperature. All of this sorbed oxygen could be removed by evacuation, in distinction to the fixation found by Langmuir, but it was not stated whether the oxygen came off as such or as oxides of carbon. The electrical resistance of the filaments was found to vary slightly with oxygen content. These results were interpreted as evidence that oxygen was able to penetrate the graphite lattice at temperatures below 1500°C .

Meyer suggested that the mechanism of oxidation at temperatures below 1450°C . is represented by the equation



while above this temperature, it may be expressed by



From the sorption measurements, and from the fact that hexagonal pits were etched in the filament surfaces, the conclusion was drawn that the low temperature reaction attacks the basal planes of the graphite lattice. Two molecules of oxygen are supposed to be sorbed on or dissolved in the lattice, possibly according to the scheme represented in figure 4, in which the apices of the hexagons represent carbon atoms and the dotted lines represent bound oxygen atoms. This sorption or solution causes an acti-

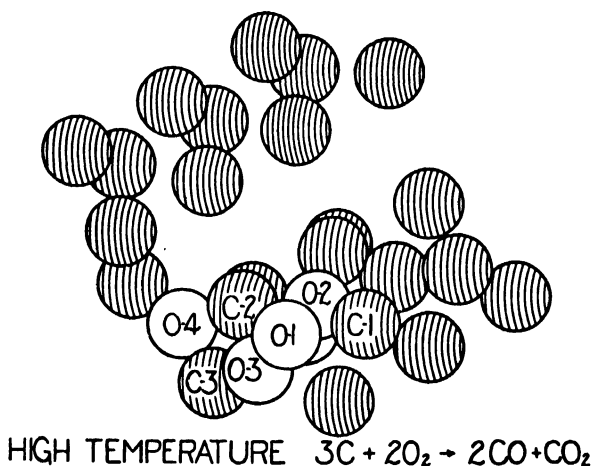


FIG. 5. MECHANISM OF COMBUSTION ACCORDING TO A. EUCKEN

Shaded spheres represent carbon atoms in hexagonal array extending indefinitely upward and to the right. Unshaded spheres represent oxygen atoms adsorbed on edges of the carbon lattice. In decomposing C-1 goes with O-2, C-2 with O-1 and O-4, and C-3 with O-3, giving $2CO + CO_2$.

vation of a region so that when a molecule of oxygen from the gas space impinges on this region four carbon atoms with their sorbed oxygen react according to equation 1. Above about 1250°C . the sorption of oxygen necessary for this reaction begins to fall off, until above 1450°C . it can no longer occur and the second type of reaction takes its place. For the latter, Meyer adopted the interpretation offered by Eucken (8) in connection with Sihvonen's experiments. The reaction was assumed to occur through the sorption of oxygen on the few very active spaces in the neighborhood of corner and edge atoms of the lattice, as shown in figure 5. The zero order of the reaction was explained by the large energy of binding of oxygen on these active spaces, since it would necessitate an average

life of sorbed molecules considerably greater than the time between collisions. The temperature coefficient indicates an activation energy for the high temperature reaction of the order of 90 kilocalories, which is of the same order of magnitude as the heat of sorption of the first increments of oxygen admitted to a clean carbon surface (11, 14).

More recently, Sihvonen has given a lengthy, largely theoretical discussion (28) of possible reactions of oxygen on graphite surfaces. While he agrees with Meyer in believing that some sort of specific binding of oxygen with solid carbon exists, he does not consider that the reaction represented by equation 1 is of as great importance as that represented by equation 2. His discussion does not involve so limited a mechanical picture as does Meyer's, and may be more generally acceptable.

The low pressure experiments described above make the conclusion inevitable that the combustion of carbon by gaseous oxygen at high temperatures involves the fixing of oxygen in some strongly held complex, which then breaks down to the two gaseous oxides. Although the experimental evidence is not yet unambiguous on this point, there is some reason for believing that the complex may be regarded as an intermediate compound whose decomposition produces the gaseous oxides in fixed proportions.

II. EXPERIMENTS AT NORMAL PRESSURES

Early workers (7, 10, 16) on combustion conducted experiments at atmospheric pressures and at low temperatures, usually below 500°C. Rhead and Wheeler (25) circulated air or oxygen through a bed of charcoal which had previously been cleaned up by evacuation at high temperature. Their results showed that the first oxygen admitted does not immediately appear as gaseous oxides, that both carbon dioxide and carbon monoxide appear in the products of combustion at all temperatures, with increasing percentages of carbon monoxide as the temperature is raised, and that carbon monoxide is formed faster than it could have been liberated by the reduction of carbon dioxide. These data led them to the earliest expression of the theory of the formation of a strongly held oxide layer, to which they gave the general formula C_xO_y , as a necessary step in the combustion of carbon.

Various empirical indications of the speed of this reaction on different forms of carbon have been used for routine determinations of the combustibility of cokes. In all of these tests a standard amount of powdered coke is heated in a stream of air or oxygen and the combustibility measured by determining the ignition point (1, 3, 24), or determining the amount of carbon dioxide formed at a given temperature (6, 15). These tests give some sort of comparison of the speed of the surface reaction of oxygen on carbon, but the values obtained depend on the geometry of the apparatus, and are not suitable for calculations of the kinetics of the process.

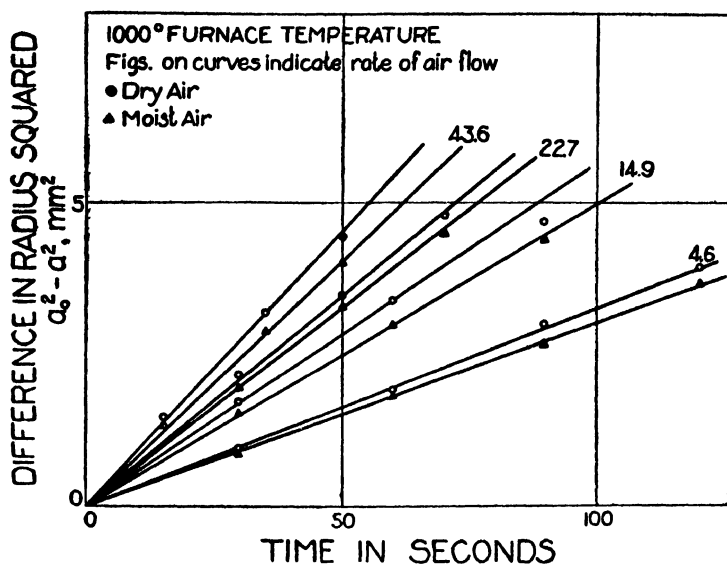


FIG. 6. PROGRESS OF COMBUSTION AT VARIOUS GAS VELOCITIES AT 1000°C.
(Smith and Gudmundsen)

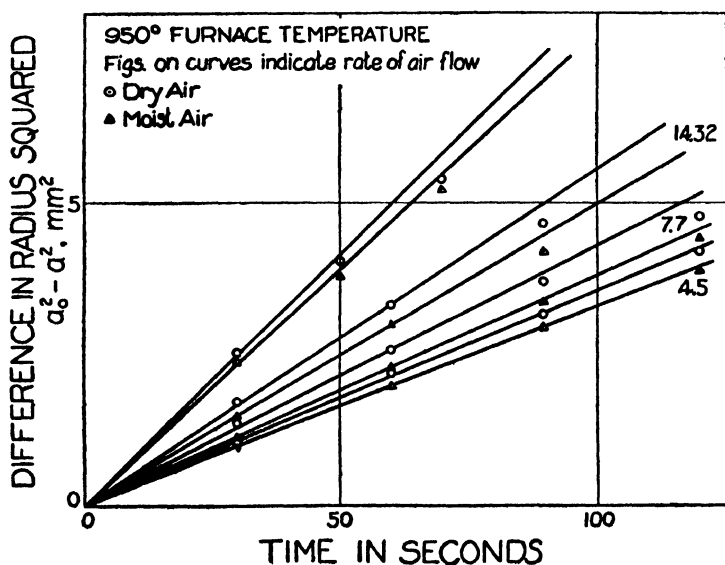


FIG. 7. PROGRESS OF COMBUSTION AT VARIOUS GAS VELOCITIES AT 950°C.
(Smith and Gudmundsen)

The later experimental work, stimulated by the increasing industrial use of pulverized fuel, was concerned with the determination of combustion rates under conditions approximating those of commercial furnace practice. Under these conditions the fuel temperature is so high that the rate of the chemical reaction at the fuel surface is very great and the speed of combustion is limited by the much slower rate of diffusion of oxygen to the fuel. Griffin, Adams, and Smith (12) arranged to photograph, on moving film, particles of pulverized fuel, of sieve sizes through 45 on 50 mesh, and through 80 on 90 mesh, as they fell through a vertical furnace open to the atmosphere. They assumed that the time of combustion was coincident

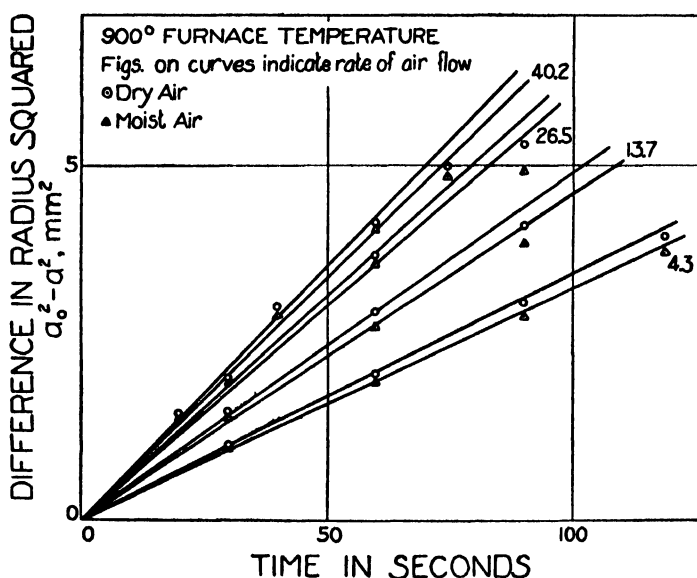


FIG. 8. PROGRESS OF COMBUSTION AT VARIOUS GAS VELOCITIES AT 900°C.
(Smith and Gudmundsen)

with the period of incandescence of a fuel particle, but, as the results determined on this basis are very erratic and the time of combustion of a given size of particle was found to increase greatly with furnace temperature, a result which disagrees with later experiments (29), this assumption is probably not justified.

Subsequently, spheres of electrode carbon, 4.6 mm. in diameter, were burnt in flowing air by Smith and Gudmundsen (29). Arrangements were made to follow the course of combustion by quenching the sample in nitrogen after definite periods of time, and weighing; and to follow the temperature of the sample surface during the burning by the use of an optical pyrom-

eter. Experiments were made using both wet and dry air, at furnace temperatures of 900°, 950° and 1000°C., and with gas velocities ranging from 1.09 to 10.25 ft. per second measured at 24°C. The particle sizes and air velocities used make the data applicable to the case of lump coal burning on a grate, but are too great for the conditions of pulverized fuel firing. Smith and Gudmundsen presented their results in terms of the "specific reaction rate," k_s , in milligrams of carbon burnt per second per square millimeter of surface, but the data have been recalculated for this paper to give

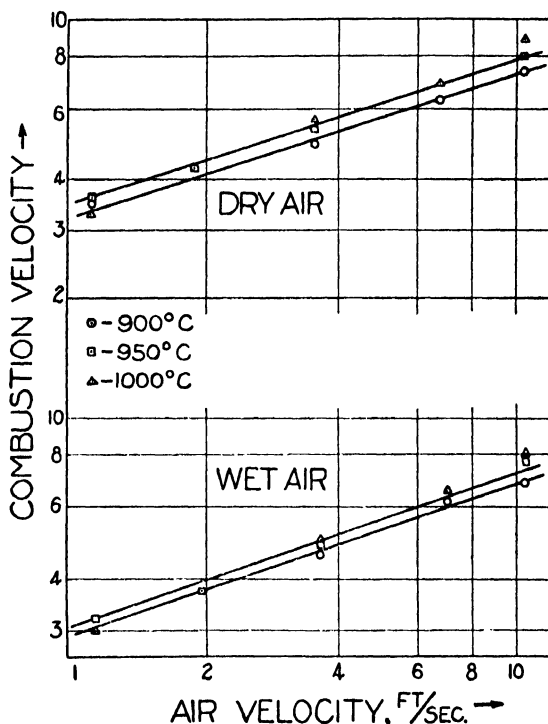


FIG. 9. VARIATION OF COMBUSTION RATE WITH GAS VELOCITY

figures 6, 7, and 8, in which the decrease in the square of the radius of the sample is plotted against the time of burning. The slopes of these curves give the combustion rate at unit radius. These may be plotted against the gas velocity on logarithmic scales as in figure 9, giving approximately straight parallel lines with a slope of 0.4. The effect of temperature on the combustion rate can not be determined from these experiments, since no consistent relation between the variables appears when they are plotted as in figure 10.

C. M. Tu (30) determined rates of combustion by weighing continuously

on a recording balance 1-inch diameter electrode carbon spheres suspended in a furnace through which were passed air and other oxygen-nitrogen mixtures at various rates of flow. In these experiments the spheres were not much reduced in size, so the variation of combustion rate with radius is not apparent. The rates of combustion, which were reported as the specific reaction rate, k_s , were directly proportional to the oxygen pressure. The values of k_s for air are plotted to logarithmic scales against velocity in figure 11. The slope of the high temperature curves has the value 0.42,

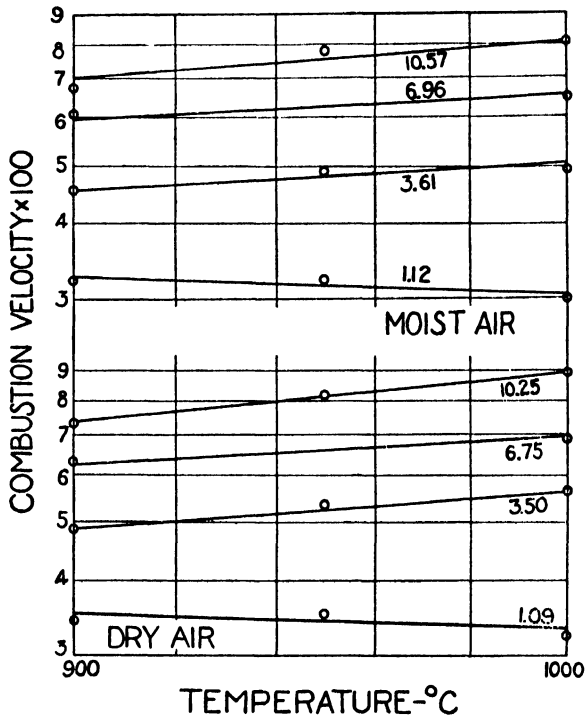


FIG. 10. VARIATION OF COMBUSTION RATE WITH TEMPERATURE

in close agreement with the slope found for the combustion rate-velocity curves representing Smith and Gudmundsen's data. In figure 12 the combustion rates are plotted against temperature, the numbers on the curves giving the velocity of air flow past the sample. Tu pointed out that the shape of these curves suggests that the combustion process consists of two types of action, the surface reaction and diffusion, in series, and that the over-all speed of combustion is determined by the slower. In the low temperature region the combustion rate has a temperature coefficient such that when $\log k_s$ is plotted against $1/T$ as in figure 13 a straight line is ob-

tained corresponding to an activation energy of about 35 kilocalories, a value not very different from that found by Meyer (22) for the surface reaction. Such a large temperature coefficient is characteristic of a chemical reaction, which, evidently, is slow enough in this region to permit oxygen to diffuse to the surface as fast as it is used without a great lowering of its partial pressure. As the temperature is increased the speed of chemical reaction increases, reducing the pressure of the oxygen at the fuel surface and increasing the concentration gradient, so that the rate of

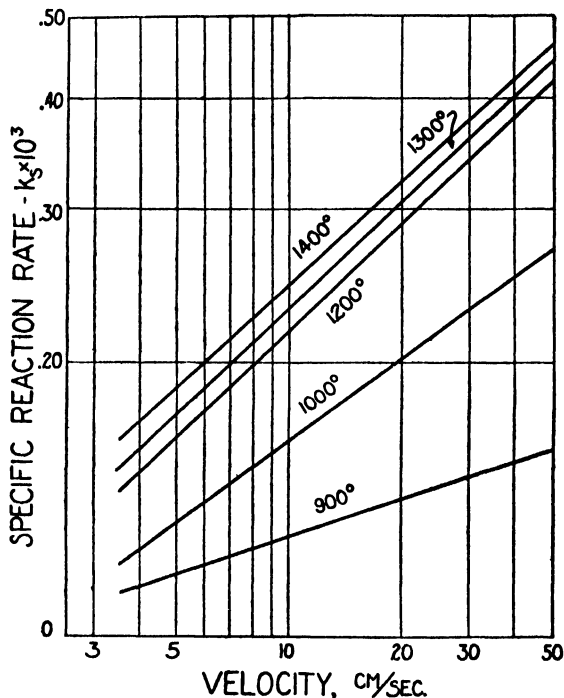


FIG. 11. VARIATION OF COMBUSTION RATE WITH GAS VELOCITY AT VARIOUS TEMPERATURES

(C. M. Tu)

diffusion becomes an increasingly important factor in determining the combustion speed. Figures 11 and 12 show that, in the high temperature range, the combustion rate has a small temperature coefficient and a large velocity coefficient, in agreement with the characteristics to be expected of such a physical process as diffusion.

III. ANALYSIS OF THE COMBUSTION PROCESS

Several workers (4a, 4b, 5, 19, 23, 30) have calculated rates of combustion on the assumption that the rate of diffusion of oxygen to the carbon

surface and of the products of combustion away from it governed the speed of the process. For this purpose it must be assumed, first, that at any time the coördinates have the values they would reach if a steady state existed, even though the boundary condition changes with time; and, second, that the rate of reaction of oxygen with a carbon surface under the conditions of combustion is great enough to reduce the partial pressure of oxygen at the fuel surface considerably below that in the atmosphere at a distance from the surface. The fundamental differential equation amounts

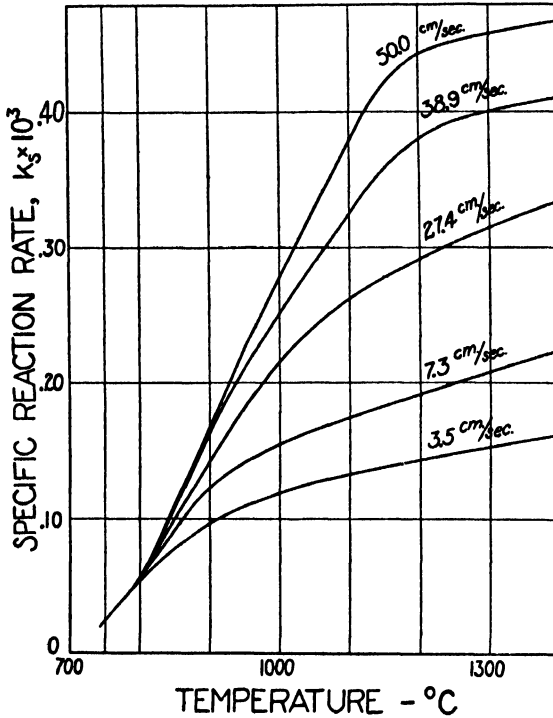


FIG. 12. COMBUSTION RATES AT VARIOUS TEMPERATURES AND GAS VELOCITIES
(C. M. Tu)

to the statement that the increase in any constituent by flow or diffusion through the boundaries of an infinitesimal element of volume is exactly balanced by the decrease of that constituent by reaction within the volume element. That is,

$$\frac{1}{r^2} \frac{\partial}{\partial r} \left[\frac{r^2}{RT} \left(D_i \frac{\partial p_i}{\partial r} + p_i V_r \right) \right] + \frac{1}{r^2 \sin \theta} \frac{\partial}{\partial \theta} \left[\frac{\sin \theta}{RT} \left(D_i \frac{\partial p_i}{\partial \theta} + r p_i V_\theta \right) \right] = -A_i f(p_1, p_2, p_3, T) \quad i = 1, 2, 3 \quad (3)$$

$$\frac{1}{r^2} \frac{\partial}{\partial r} \left[r^2 \left(k \frac{\partial T}{\partial r} + \frac{pc_r}{R} V_r \right) \right] + \frac{1}{r^2 \sin \theta} \frac{\partial}{\partial \theta} \left[\sin \theta \left(k \frac{\partial T}{\partial \theta} + r \frac{pc_r}{R} V_\theta \right) \right] = -Hf(p_1, p_2, p_3, T) \quad (4)$$

where r, θ = usual spherical coördinates.

p_i = partial pressures of oxygen, carbon dioxide, and carbon monoxide, when $i = 1, 2$, and 3 , respectively.

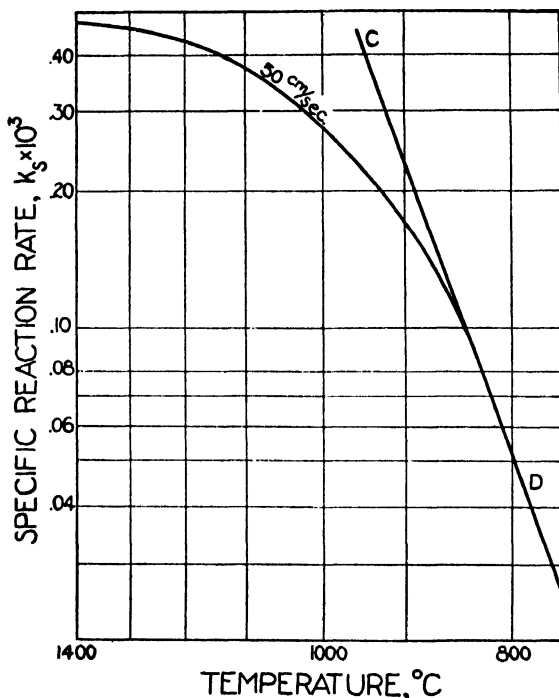


FIG. 13. EFFECT OF TEMPERATURE ON REACTION RATE

Line CD, coincident with experimental curve below 850°C., corresponds to activation energy of 35 kilocalories. Departure of experimental line from CD above 850°C. indicates effect of diffusion.

T = absolute temperature.

D_i = coefficient of diffusion associated with particular gas under discussion.

$V_{r,\theta}$ = components of gas velocity.

f = function expressing the dependence of the rate of the homogeneous reaction on the concentration of the reactants and the temperature.

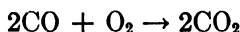
k = coefficient of thermal conductivity of the gas.

c_p = specific heat at constant pressure of the gas mixture.

H = heat of the homogeneous reaction.

$A_{CO} = -A_{CO_2} = 1$, $A_{O_2} = \frac{1}{2}$ = molar ratios in which the constituents enter the homogeneous reaction.

This equation has not yet been solved, not only because of its complexity, but also because of the uncertainties of the form of " f ," the expression for the unknown rate of the non-explosive homogeneous reaction:



and of the character of the flow of the atmosphere about a burning particle which determines the " V 's." Nevertheless, it is possible to show that the rate of combustion is given by the rate of diffusion through a surface surrounding a fuel particle at a great distance from it with the permissible assumption that " f ," the rate of the homogeneous reaction, is finite only at small distances from the particle, and becomes very small everywhere else. For, adopting vector notation, equations 3 and 4 may be expressed as

$$\nabla \cdot \left[\frac{1}{RT} (D_i \nabla p_i + p_i \mathbf{V}) \right] = -A_i f \quad (5)$$

$$\nabla \cdot \left[k \nabla T + \frac{p c_p}{R} \mathbf{V} \right] = -Hf \quad (6)$$

The rate of use of oxygen in the homogeneous reaction is given by

$$\int_{\tau} A_1 f d\tau$$

where τ represents the volume inside a large surface S which is everywhere distant from the fuel surface. Substituting its equal from equation 5 for $A_1 f$ we have, by Gauss' theorem,

$$\begin{aligned} - \int_{\tau} \nabla \cdot \left[\frac{1}{RT} (D_1 \nabla p_1 + p_1 \mathbf{V}) \right] d\tau &= - \int_S \frac{1}{RT} (D_1 \nabla p_1 + p_1 \mathbf{V}) \cdot d\mathbf{S} \\ &+ \int_s \frac{1}{RT} (D_1 \nabla p_1 + p_1 \mathbf{V}) \cdot d\mathbf{s} \end{aligned} \quad (7)$$

where \mathbf{s} represents a surface at an infinitesimal distance outside the fuel surface. Now, the boundary condition representing the rate of reaction of oxygen with the carbon surface is given by

$$- \int_s \frac{1}{RT} (D_1 \nabla p_1 + p_1 \mathbf{V}) \cdot d\mathbf{s} \quad (8)$$

Hence the total rate of use of oxygen is given by the sum of equations 7 and 8 or

$$K_{O_2} = - \int_S \frac{1}{RT} (D_1 \nabla p_1 + p_1 \mathbf{V}) \cdot d\mathbf{S}$$

If S be taken as a sphere of radius B , where B is very large, $V_r = V \cos \theta$ and T is constant everywhere on S . Since only diffusion or gas velocity along the normal to the surface make contributions to K_{O_2} , we have

$$\begin{aligned} K_{O_2} &= \int_0^\pi \frac{1}{RT} \left[\left(D_1 \frac{\partial p_1}{\partial r} + p_1 V \cos \theta \right) 2\pi r^2 \right]_{r=B} \sin \theta \, d\theta \\ &= \frac{4\pi D_1}{RT} \left(r^2 \frac{\partial p_1}{\partial r} \right)_{r=B} + 2\pi \int_0^\pi [p_1 r^2 V]_{r=B} \cos \theta \sin \theta \, d\theta \end{aligned} \quad (9)$$

Since in most cases, the combustion of a single particle does not change appreciably the concentration of oxygen in the stream of gas flowing past it, p_1 in the second integral is constant with respect to θ and the integral vanishes since $\int_0^\pi \cos \theta \sin \theta \, d\theta$ vanishes, whence

$$K_{O_2} = \frac{4\pi D_1}{RT} \left(r^2 \frac{\partial p_1}{\partial r} \right)_{r=B} \quad (10)$$

This conclusion is of enhanced importance since its experimental verification is possible; if the concentration gradient close to the combustible were required, it would not be.

The analysis given above does not eliminate the necessity of solving the differential equations, since this is necessary to obtain $\left(r^2 \frac{\partial p}{\partial r} \right)_{r=B}$. In the simplest possible case, assuming first, that there is no homogeneous reaction, i.e., that $f = 0$ everywhere, and the carbon burns directly to carbon dioxide; second, that the surface reaction is so fast that the partial pressure of oxygen at the surface is sensibly zero; third, that there is no flow of gas about the fuel; and fourth, that the temperature is everywhere constant; the differential equations reduce to

$$\frac{d}{dr} \left(r^2 D \frac{dp}{dr} \right) = 0$$

whence

$$p = \frac{C_2}{r} + C_1$$

and, introducing the boundary conditions,

$$p = P_1 - \frac{aP_1}{r}$$

where P_1 = partial pressure of oxygen in the ambient atmosphere and a = radius of the particle. Then the combustion rate, in grams of carbon, is

$$K = 12 \left[4\pi \frac{D}{RT} \left(r^2 \frac{dp}{dr} \right) \right]_{r=\infty} \quad (11)$$

$$= 12 \left[4\pi a \frac{D}{RT} P_1 \right]$$

The temperature restriction may be removed by assuming that the coefficient of diffusion, D , and the thermal conductivity follow the laws

$$D = D_{i_0} \left(\frac{T}{T_0} \right)^2 = D_1 T^2$$

where

$$D_1 = \frac{D_{i_0}}{T_0^2}$$

and

$$k = k_0 \left(\frac{T}{T_0} \right)^{1/2} = k_1 T^{1/2}$$

where

$$k_1 = \frac{k_0}{T_0^{1/2}}$$

where D_{i_0} , k_0 = values of the constants at T_0 = some arbitrary temperature. Then, by methods analogous to those used in obtaining equation 11

$$K = 12 \left[4\pi a \frac{D_1 P}{R} \frac{T_2 + T_1 + \sqrt{T_1 T_2}}{3} \right] \quad (12)$$

where, if it be assumed that the particle loses heat only by conduction through the gas about it, T_2 is given by

$$T_2^{1/2} - T_1^{1/2} = \frac{D_1 P H_1}{2Rk_1} \quad (13)$$

whence the temperature of the particle does not vary with its radius; while, if it be assumed that the particle may lose heat by radiation as well as con-

duction, as for particles at the outside of a pulverized fuel flame and also in Smith and Gudmundsen's experiments, T_2 is given by

$$\frac{T_2^4 - T_1^4}{T_2^{3/2} - T_1^{3/2}} = \frac{1}{4\pi\sigma a} \frac{D_1 P H_1}{3R(T_2^{1/2} - T_1^{1/2})} - \frac{2k_1}{3} \quad (14)$$

where H_1 = molar heat of combustion of carbon and σ = radiation constant in the Maxwell-Boltzmann law.

It is to be noted that, whether variable temperature be considered or not, the rate of combustion is proportional to the partial pressure of the oxygen and to the radius of the fuel particle. The former result was verified experimentally by Tu, and the latter is confirmed by the work of Smith and Gudmundsen. The curves of figures 6, 7, and 8 may be expressed approximately by the equations

$$(a_0^2 - a^2) = \frac{M}{2\pi\epsilon} t \quad (15)$$

where t = time,

ϵ = density of the fuel,

M = combustion rate constant, and

a_0 = radius of the particle at time zero.

Differentiating, and multiplying through by a , we have

$$-4\pi\epsilon a^2 \frac{da}{dt} = Ma$$

But the rate of combustion is the rate of decrease in weight of the particle, whence

$$K_{\text{obs.}} = -4\pi\epsilon a^2 \frac{da}{dt} = Ma \quad (16)$$

The correctness of the temperature dependence of the combustion rate given by equations 12, 13, and 14 is more difficult to evaluate. For the condition of no radiation, K varies with a power of T_1 between 1 and $\frac{1}{2}$. Tu's experiments, which were so arranged as to approximate this condition, indicate that the combustion rate varies as the 0.42 power of the temperature, as indicated by figure 14. Tu's calculations, based on finite film theory, agreed well with this temperature dependence, giving T the exponent 0.37, represented by the slope of the line AB. When radiation occurs, K , as represented by equations 12 and 14, varies as a power of T_1 slightly greater than 1, which is in agreement with the somewhat inconsistent results of Gudmundsen and Smith shown in figure 10.

Burke and Schumann (4a, 4b, 5) and Tu (30) attempted to remove the

restriction of zero gas velocity by considering the particle to be surrounded by a finite film of stagnant gas whose thickness was calculated from Rice's formula (26) which was developed to account for the phenomena of heat transfer. While the existence of a stagnant fluid film is extremely doubtful (9, 13), the use of the concept for purposes of calculation has been fruitful in the field of heat transfer. Times of combustion calculated according to the method of Burke and Schumann (4b) have been plotted against the square of the particle radius in figure 15 for comparison with the data for dry

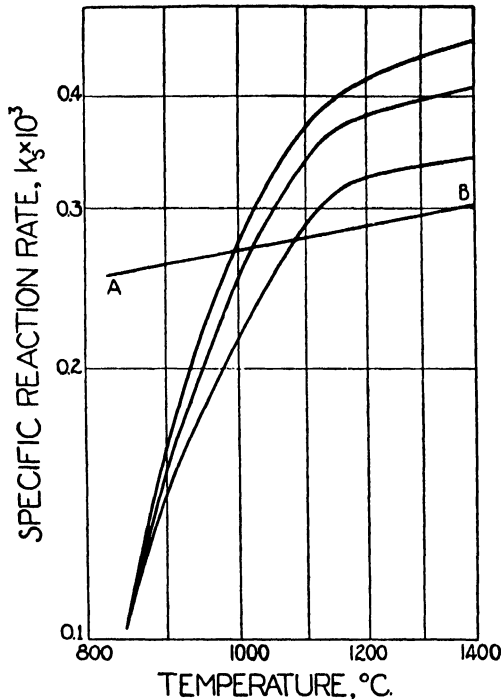


FIG. 14. EFFECT OF TEMPERATURES ON DIFFUSION RATE

Line AB corresponds to the temperature coefficient calculated for diffusion effect by C. M. Tu.

air in figure 6. The lines have a definite curvature, but this is in such a direction as to include the few points that fall off the straight lines of figure 6. If the deviations of those points from linearity are not due to experimental errors, the form of the Burke and Schumann equations, which give values of the combustion rate not exactly proportional to the radius for small particle sizes, is evidently more nearly correct, although the absolute values of the time of combustion are 60 per cent greater than those observed. This discrepancy may be due to the uncertainty of the values of diffusion

coefficients at the high temperatures involved, and of the correct values of the constants in the formula for the effective film thickness. In making similar calculations, Tu found it necessary to modify both the coefficient and the exponent of the Reynolds number in Rice's formula in order to obtain satisfactory agreement with his experimental data.

Burke and Schumann (5) also tried to remove the restriction concerning the homogeneous reaction by postulating the existence of a double film. In the outside film carbon dioxide diffused outward, while oxygen passed inward to the boundary of the inner film where it met and burned carbon monoxide diffusing out. The carbon monoxide was formed at the fuel surface by the reduction of carbon dioxide, which diffused inward through

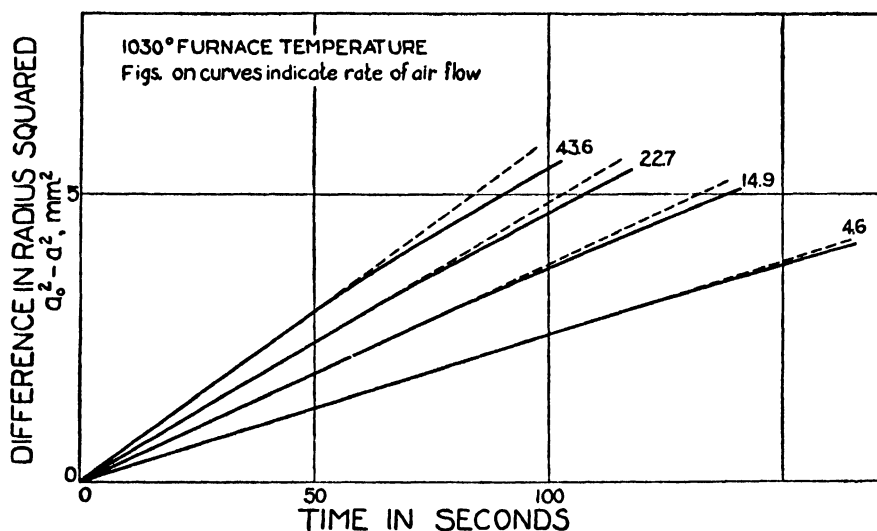


FIG. 15. PROGRESS OF COMBUSTION CALCULATED ACCORDING TO BURKE AND SCHUMANN

Dotted lines are straight, corresponding to lines of figure 6

the inner film. This mechanism can not be accepted because of the fact that even if the partial pressure of carbon dioxide at the fuel surface were as great as that of oxygen in air, which is its maximum possible value, the rate of gasification of carbon, according to measurements (20) made in this laboratory, would be not more than 1/50 of the observed rates of combustion.

Indeed, the work of Meyer indicates that, even with oxygen, an appreciable pressure at the carbon surface may be required to account for observed rates of reaction. The maximum value of k , reported by Smith and Gudmundsen is in the neighborhood of 0.05 mg. of carbon burned per second per square millimeter at the highest air velocity with a furnace tempera-

ture of $1000^{\circ}\text{C}.$, when the sample temperature was about $1530^{\circ}\text{C}.$ At about this temperature, Meyer found a zero order reaction in which 0.047 mg. of carbon was burned per square centimeter per minute, a value only $1/6400$ of that found at normal pressure. Two possibilities may account for this discrepancy. The reaction described by Meyer as of zero order may be of the first order; then, since the pressure at which the measurements were made was about 10×10^{-3} mm., a pressure of about 10 mm. would be required to bring the results into approximate accordance. On the other hand, Smith and Gudmundsen's temperature measurement may have determined not that of the particle surface, but the temperature of the flame of carbon monoxide formed by the primary reaction. In this case, if the surface temperature had been as low as $1250^{\circ}\text{C}.$, the first order reaction described by Meyer could take place and a pressure of the order of 100 mm. would be required. This would certainly be great enough to invalidate the assumption of very small oxygen pressure at the fuel surface; and the rate of diffusion of oxygen and, hence, the combustion rate would not be proportional to the atmospheric oxygen pressure, but to the difference between that and the pressure at the fuel surface. However, in view of the agreement found between calculations based on previous assumptions and experimental data, it seems wise to suspend acceptance of the rates of the high vacuum oxidation until these are confirmed.

The foregoing discussion indicates that with the help of certain assumptions equations may be derived which, although they are rather unwieldy, give qualitative agreement with the effects of changes in the variables on the rate of combustion. Apparently because of uncertainties of the values of certain physical constants at the high temperatures involved, the agreement of the calculated rates with observed ones is only qualitative. This fact, combined with the uncertain validity of the assumptions involved in the derivation, justifies the use of an empirical formula based on the data discussed above and not in conflict with any theoretical considerations. This formula gives the rate of combustion, in milligrams of carbon per second, of a sphere in a high velocity stream of air at high temperature, as follows

$$K = 4\pi\epsilon a^2 \frac{da}{dt} = 0.068 \left(\frac{P_1}{0.21} \right) \left(\frac{T}{1273} \right)^n V^{0.4} a \quad (17)$$

In this expression P_1 is to be measured in atmospheres, V is the air velocity in centimeters per second at normal temperature and pressure, and a , the radius of the particle, is to be measured in millimeters. The value of n is rather uncertain and may be between $1/2$ and $3/2$, although for many cases it is probably nearly equal to 1. The formula should be applied only

with reservations to the calculation of combustion rates under conditions differing greatly from those of the experiments of Smith and Gudmundsen.

CONCLUSIONS

Various experimental determinations of the mechanism and rate of combustion of solid carbon by gaseous oxygen have been reviewed, and previous mathematical analyses of the process have been discussed.

The nature of the primary reaction between graphitic carbon and oxygen has been considered on the basis of experiments made at such low gas pressures that diffusion effects were eliminated: These experiments have been shown to indicate that combustion involves the formation of a strongly held oxide or sorbed oxygen layer on the carbon surface. It has also been shown, however, that these high vacuum measurements of the rate of oxidation can not be brought into agreement even in order of magnitude with the rates determined at ordinary pressures.

It has been shown that, for ordinary industrial furnace conditions, the assumption that the rate of diffusion of oxygen to the fuel surface limits the speed of combustion, permits the calculation of combustion rates, which agree, both in order of magnitude and in the effect of changes in the variables, with observed rates. However, mathematical difficulties prevent a rational solution of the equations governing the process, so that the best expression that can be offered is the largely empirical one

$$K = 0.068 \left(\frac{P_1}{0.21} \right) \left(\frac{T}{1273} \right)^n V^{0.4} a$$

where the value of n is probably between $1/2$ and $3/2$.

It may be concluded, then, that no complete formulation of the rates or mechanism of the combustion of carbon is yet possible. More experimental measurements at very low pressures are needed to resolve the discrepancy between the rates of the surface reaction already observed, and those known to occur in ordinary combustion. The experimental work at normal pressures must be extended over a much wider range of temperatures, pressures, sizes of combustible sample, and gas velocity—the latter especially toward the low velocity region to secure information concerning the conditions that govern powdered coal firing—and the work should be so arranged that constants required for the mathematical formulations may be secured. Last, a solution of an inhomogeneous differential equation of the second order is required before the experimental work can be expressed in its most complete form.

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ORIENTING INFLUENCES IN THE BENZENE RING

A REVIEW OF EXPERIMENTAL EVIDENCE

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The entry of a second group or radical into the nucleus of a monosubstituted benzene is well characterized by the lack of random in respect to the position attacked. Indeed, such apparently is also the case for any aromatic substitution reaction in which there are one or more substituents present and two or more positions open to substitution. Thus it is a very general phenomenon and one of no slight complexity. In its simplest form, where a single substituent enters the ring of a monosubstituted benzene, it is the fact that all three possible isomers are not formed in equal amounts which gives rise to this problem. (It is to be noted that possibly twice as much of the ortho and meta isomers as of the para isomer would be the normal circumstance in the absence of directive influences.) Furthermore, the ratio of isomers formed varies enormously with the character of the original substituent. These facts summarize briefly the well-known problem of orienting influences in the benzene ring.

That each aromatic substituent possesses a characteristic directive influence has been known for many years, and not a few hypotheses have been offered to explain the observation that a group was either ortho-para or meta directing. But it is not easy to classify the many substituents in this way, for an almost infinite variation in the ratios of the isomers is apparently possible. Though such a situation is caused in large measure by the great number of possible substituents, there are other factors as well. The influence of temperature, reaction medium, and catalysts should not be heedlessly neglected. The rôle of these factors and the consequent difficulty of attaining comparable reaction conditions for the estimation of the relative directive strengths of various substituents has

¹ The major part of this paper was accomplished while the author was at The Johns Hopkins University. Revision and additions were made during the course of his work at The Victoria University of Manchester, Manchester, England, as a Senior Fellow of The Textile Foundation of Washington, D. C. Present address, Massachusetts Institute of Technology, Cambridge, Massachusetts.

been emphasized by Holleman (97). In view of such difficulties and the fact that every case of aromatic substitution bears evidence upon the question, it is not surprising that in the many years no final or generally accepted solution to the problem has been attained.

In recent years both the theoretical and experimental aspects have been developed and much has been accomplished. Of particular value is the full appreciation of the fact that the problem is fundamentally one of reaction rates. But it is not the purpose of this paper to discuss either the theory or the relative merits of the various hypotheses. Excellent reviews of this nature have been done by Holleman (97), by Francis (67), and by Stewart (191). On the other hand, it is believed that a presentation of the collected experimental evidence may be of some interest and value.

The extent of such an undertaking was fully appreciated. At the same time it is possible to gain a real understanding of the problem from a fairly limited field. Thus by considering only the entry of a second substituent into the ring of monosubstituted benzenes, we take certainly the most fundamental if not the simplest aspect of the problem. Yet even then the possible number of substituents is almost numberless and consequently only the simplest and most significant ones can be considered here. Obviously, a choice must be made from among those of which definite information concerning orienting influences is available. The following nine substituents have been selected: $-\text{COOH}$, $-\text{NO}_2$, $-\text{SO}_3\text{H}$, $-\text{CH}_3$, $-\text{OH}$, $-\text{NH}_2$, $-\text{Cl}$, $-\text{Br}$, and $-\text{I}$. Except for the first three, they represent the simplest types of substituents. The three exceptions are chosen primarily because they are perhaps the most striking of meta orienting substituents, and in the case of $-\text{SO}_3\text{H}$, because no satisfactory or direct evidence concerning the orienting influence of its parent group, $-\text{SH}$, is available. On the whole, these nine substituents are surely a representative series, since all of the other possible groups may be considered as their derivatives.

Substituents such as $-\text{HgCl}$, in which a group is attached through a metallic element, and other similar possible groups are not considered here since their orienting influences have not been satisfactorily studied. Actually, the carboxyl, nitro, and sulfonic acid radicals might be omitted, for they are obviously derivatives of simpler groups. As for their meta orienting nature, it will appear later that under certain conditions even their parent groups may become meta orienting, or they themselves para or ortho orienting. To continue, however, there is similarly almost no limit to the type of group which may be introduced into the benzene ring, as a second substituent. Therefore, only three types of secondary substitution, namely, halogenation (exclusive of fluorination), nitration, and sulfonation have been chosen. Once again the problem so limited is by no means satisfactory, yet it is concerning these types of substitution reactions

only that sufficient evidence is available. It is true, of course, that much study has been devoted to the introduction of alkyl, amino, hydroxy, and carboxyl groups, and even to mercurization, yet the information is relatively meagre and the methods vary so as to offer no satisfactory standard for comparison. Thus, within the three carefully chosen limitations, the immediate problem is clearly set forth, principally to seek what information in each case is offered in the literature concerning the relative proportion in which the isomers of disubstituted benzenes are formed. Now, although such is actually the heart of the problem, it must be recognized that other factors play an important rôle. Hence it will be with especial regard to reaction conditions that the present examination of the experimental facts is undertaken.

Although it is hoped by such an attempt to arrive at some general conclusions, the main object nevertheless must be the presentation of a comprehensive review of the relevant facts. Yet in doing so there are many investigations which add nothing new or significant or which have been greatly enlarged or improved upon by later studies. Consequently, much has been omitted from the text, but in order to accomplish the intended purpose these studies are given in the supplementary references at the end of this article. In this way it is hoped that this paper will prove to be a ready source of information for all interested in this problem, as well as a contribution to the theoretical aspect of the question. The material is arranged according to the nine substituents and in the order as given above. Finally some attention will be devoted to derived substituents and to the rôle of molecular rearrangements.

THE CARBOXYL SUBSTITUENT: BENZOIC ACID

Benzoic acid, the benzene derivative containing the carboxyl group as a single substituent, has been chlorinated to give chlorobenzoic acid by a number of workers. The first satisfactory investigation was that of Beilstein and Schlumm (25). Chlorinating with potassium chlorate and hydrochloric acid they obtained principally the *m*-chlorobenzoic acid. Their work was later supplemented by Claus and Buecher (35) who, using the same method, showed that some of the ortho isomer also resulted. Similarly, the use of either antimony pentachloride or calcium chloride, according to Holleman (98), will give the same isomers. On the other hand, Lossen found that a hypochlorite in a dilute aqueous solution of benzoic acid at a temperature under 50°C. will give the *o*-chlorobenzoic acid with some of the para and a smaller quantity of the meta isomer. But with calcium chloride, the same worker obtained principally the para isomer together with some of both the meta and ortho isomers (98). Again, the use of sodium hypochlorite gave Lossen nearly equal amounts of the ortho and para derivatives (98).

Furthermore it is of some interest that Pisoni in 1847 chlorinated benzoic acid in a solution of excess caustic potash with chlorine gas and obtained the *o*-chlorobenzoic acid (98). In striking contrast, liquid chlorine and ferric chloride was found by Bornwater and Holleman (28) to cause meta substitution exclusively. A 95 per cent yield of the meta isomer and a little of the ortho derivative were obtained by Gluud and Kempf (80) by treatment with concentrated hydrochloric and nitric acids. Passing on to the bromination of benzoic acid, one finds that Holleman again provides information of some interest. He refers to a number of workers, showing that bromination with bromine water in a sealed tube leads principally to the meta acid and probably one or both of the other isomers (reference 98, p. 116). The probable formation of all three isomers is indicated by Claus and Reh (36) who actually obtained them on bromination with potassium bromate and hydrobromic acid in a dilute water solution at 70–80°C. Yet a quantitative yield of the metaderivative is reported by Wheeler and McFarland (208) who brominated in the presence of iron wire or gauze.

With respect to iodination, there are only four sources of information. Although the methods are quite different, the meta isomer occurred in each case. Peltzer used potassium iodate and Birnbaum and Reinherz heated silver benzoate with iodine (see reference 98, p. 118). Datta and Chatterjee (47) iodinated with iodine and nitric acid in glacial acetic acid. Finally, a good yield of the *m*-bromo- and *m*-iodo-benzoic acids was obtained by halogenation in the presence of a mixture of fuming nitric acid and nitrosulfonic acid formed by passing sulfur dioxide through fuming nitric acid until 50 per cent nitrosulfonic acid is present (203).

It is apparent that, although the carboxyl radical is considered to be a strong meta directing group as opposed to an ortho-para directing substituent, no evidence is forthcoming to prove that the meta isomer is formed exclusively as a general case. Furthermore, where the meta isomer occurs in large amounts, it is frequently accompanied by some of the ortho isomer even though para substitution is totally absent. Yet ortho substitution is generally supposed to be accompanied by para substitution. This particular case suggests that ortho substitution can possibly occur equally well with meta substitution.

But the above is not the only inference to be drawn from the evidence, for although the influence of temperature has been completely neglected, that of the reaction medium has already been pointed out by Holleman (98). He calls attention to the fact that in the case of chlorination, the meta isomer seems to be formed in acid solution, whereas the ortho and para isomers occur in neutral or basic solutions. His interpretation of these effects, however, is not necessarily correct, for it seems more probable that an alkaline medium acts to prevent meta in favor of para substitution.

In any case this particular aspect in which a complete reversal of the orienting influence is effected may be of considerable significance. In addition it must be recalled that the carboxyl group has been considered in the introduction as a derivative of the methyl radical and hence should possess on that basis a para orienting influence. As previously indicated, here is a case where a typical meta orienting substituent actually may under certain conditions cause substitution in the para position. But before taking up the nitration of benzoic acid it must be pointed out that the effect of certain catalysts is quite marked. Unfortunately no conclusions can be drawn unless one assumes that they affect the acidity of the reaction medium.

TABLE 1
Nitration of benzoic acid

NITRATION AT	ORTHO ISOMER	META ISOMER	PARA ISOMER
<i>degrees C.</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
-30	14.4	85.0	0.6
0	18.8	80.2	1.3
30	22.3	76.5	1.2

TABLE 2
Nitration of benzoic acid at 30°C.

	ORTHO ISOMER	META ISOMER	PARA ISOMER
	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
Without H ₂ SO ₄	22.3	76.5	1.2
With H ₂ SO ₄	19.6	75.5	4.9

The influence of the carboxyl group on the introduction of the nitro group has been rather successfully studied. Although the results of the many early workers are rather conflicting, a very complete investigation by Holleman (100) has made the case relatively clear. Using absolute nitric acid he obtained the results as presented in table 1. To determine the influence of sulfuric acid, Holleman (96) carried out an additional investigation, using a great excess of concentrated sulfuric acid (see table 2). In addition, however, there is another study which appears to involve a molecular rearrangement. Francis (65) found that benzoyl nitrate, C₆H₅·CO·ONO₂, when dissolved in nitrobenzene was converted after six months into *m*-nitrobenzoic acid to an extent of about 60 per cent. Holleman (reference 98, p. 128) doubts that a true molecular rearrangement has occurred in this case, since benzoyl nitrate on storage is known to decompose into benzoic anhydride and nitric acid anhydride. In any case

he states that the *m*-nitrobenzoic acid was completely free of its isomers. The exclusive formation of a single isomer suggests, however, that the change is virtually a rearrangement.

In regard to the above evidence it is hardly necessary to mention that the meta substitution which generally prevails on nitration of benzoic acid is accompanied principally by ortho substitution and to only a slight extent by para substitution. This is virtually a case of ortho-meta substitution, although, according to current theories, a substituent directs an incoming group either to the ortho and para positions or to the meta position. These experiments illustrate not only this point, but also the influence of temperature and the presence of sulfuric acid. It is readily seen that rise in temperature favors an increase in the amount of the ortho, a decrease in the amount of the meta, and a slight increase in the para isomer. Particular attention is called to this temperature effect, for, as will be seen later, it is the same in all cases except where molecular rearrangements are known to take place. With respect to the influence of sulfuric acid, it is clearly shown that more of the para isomer is formed, principally at the expense of the ortho isomer, whereas meta substitution is but slightly, almost negligibly, hindered. Although sulfuric acid exerts a similar influence in several other cases, the effect is by no means so marked as that of temperature.

Turning now to the introduction of the sulfonic acid group, one finds that though it has been variously studied, a brief examination of the bulk of the evidence proves it to be only partially understood. Recently, however, the author (169) has undertaken this problem and has been able to throw some light on the question.

Generally speaking, previous work had shown that benzoic acid might be readily sulfonated with strong sulfuric acid at high temperatures (ca. 200°C.) and by long duration of heating (two to twenty-four hours). In this way about 90 per cent of the product is the *m*-sulfobenzoic acid and the balance is the para isomer. Furthermore, Maarse (139), to whom credit for the above evidence is also due, incidental to his lengthy investigation, had demonstrated that the meta isomer may be converted under the ordinary reaction conditions into the para isomer to the extent of about 15 per cent, although the reverse reaction was found to occur to about a threefold greater degree. Besides the work of Maarse, however, there are two investigations which deserve attention. In the first of these, Holdermann (95) studied the effect of the presence of metallic sulfates, such as those of mercury, copper, cadmium, etc., and found that the sulfonation reaction was in no way influenced. In the other, Auger and Vary (8) found that sulfonation in the presence of iodine always gave a mixture of all three isomeric sulfobenzoic acids, of which the ortho acid amounted to only 1

per cent. On the other hand, the author (169) has shown that ortho substitution normally occurs even in the absence of a catalyst. Indeed this investigation indicates that the ortho isomer was formed as an intermediate product which, under the reaction conditions, was isomerized to the meta derivative to such an extent that its presence among the products could scarcely be detected. Furthermore, the reaction was definitely proved to be an indirect one, the probable scheme being the formation of an addition compound between the sulfuric acid and the benzoic acid, a condensation to form a benzoylsulfuric acid, followed by an isomerization to the *o*-sulfobenzoic acid and thence to the meta isomer. Other evidence, especially that provided by Maarse (see above), indicates that the para acid is formed by a rearrangement of the meta acid. Briefly, therefore, the sulfonation of benzoic acid has been shown to lead principally to the meta isomer by an indirect reaction. Furthermore, a close association between the ortho and meta isomers has been shown to exist, a situation complementary to that between ortho and para isomers when aniline, toluene, and phenol are sulfonated (see later sections of this paper). This case certainly suggests again that ortho substitution may be associated not only with para but also with meta substitution. Altogether the evidence concerning the sulfonation of benzoic acid agrees well with that obtained from halogenation and nitration, except that the former appears as an indirect, and the two latter as direct, substitution reactions.

THE NITRO SUBSTITUENT: NITROBENZENE

Nitrobenzene, in which the nitro group is the substituent, has been variously halogenated but the evidence is somewhat unsatisfactory. The earliest work is that of Kekulé (126), who chlorinated with antimony trichloride in the presence of iodine and obtained mostly the *m*-chloronitrobenzene with a little of the para isomer. A few years later Laubenthal (133), chlorinating with chlorine gas in the presence of 10 per cent of iodine at temperatures slightly over 0°C., reported the formation of only the *m*-chloronitrobenzene. Beilstein and Kurbatow (24) chlorinated with antimony trichloride and chlorine, but their results add nothing to the evidence already given. The relative catalytic effect of ferric chloride, aluminum chloride, and stannic chloride was studied by Goldschmidt and Larsen (81) and the strength of these salts was found to decrease in the order given. The meta isomer was found in each case. The investigation of Scheufelen (177) is the only one available concerning the bromination of nitrobenzene. Using ferric bromide and ferric chloride to aid bromination with bromine and at temperatures from 60° to 110°C., he obtained only the meta isomer.

Only a few remarks can be offered concerning these facts. A catalyst

in the nature of a so-called halogen carrier is apparently necessary. This fact perhaps explains why the meta isomer occurs exclusive of the ortho, for such catalysts are generally known to favor strongly either the para or the meta position. Under such conditions it is not unusual that no ortho substitution has been reported. Obviously, however, the work here has not been thorough or exhaustive, and more study is certainly to be desired.

The nitration of nitrobenzene apparently offers a less difficult task than the halogenation. It has been quite successfully investigated by Holleman and de Bruyn (105). They have shown not only that meta substitution prevails nearly completely, but also that the ortho and para isomers are simultaneously formed. That considerably more of the ortho isomer occurs is of the same significance as pointed out in the case of benzoic acid. In table 3 the influence of acid strength as well as that of temperature is clearly shown. The relative proportion of isomers is seen to be but slightly

TABLE 3
The nitration of nitrobenzene

TEMPERATURE	CONCENTRATION OF NITRIC ACID	RESULTING ISOMERS			EXTENT OF NITRATION
		Ortho	Meta	Para	
<i>degrees C.</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	
0	98.58	6.4	93.2	0.25	Complete
30	94.50	8.1	91.2	0.7	Incomplete
30	95.90	8.5	91.0	0.5	Incomplete
30	97.6	8.1	90.9	1.0	Complete
0	98.58 (H ₂ SO ₄)	4.8	93.5	1.7	Complete
40	97.6 (H ₂ SO ₄)	6.8	91.8	1.4	Complete

affected by the acid strength in the experiments at 30°C. The time required for nitration is however strongly influenced, for with 94.5 per cent and 95.9 per cent acid, it is still incomplete, whereas with 97.6 per cent acid this is not so. In another place Holleman (reference 98, p. 71) gives more data. The nitration with 94.5 per cent acid required 11½ hours to give a 67.1 per cent yield of the dinitro product, whereas nitration with the 95.9 per cent acid requires but 2 hours to yield up to 73.2 per cent of the theoretical quantity. He ascribes the fact that the smaller degree of nitration requires more time to the difference in water content between the two acids used, amounting to only 1.4 per cent. Holleman also concludes that, since the time required for nitration does not appreciably change the relative proportion of the isomers, they are formed at equal reaction rates. In addition to the effect of acid strength or presence of water, a rise in temperature is seen to cause the usual increase in the ortho isomer, the considerably smaller increase in the para, and the decrease in the meta isomer. When

sulfuric acid is present, the temperature effect is not so great, but the amount of para isomer formed is nevertheless greater than when nitric acid alone is used. The sulfuric acid, like the rise in temperature, is thus seen to exert its usual effect.

Although the above study is quite satisfactory, there are several more investigations which deserve attention. In one, the effect of mercuric nitrate has been studied by Holdermann (95); its only effect was found to be to increase the yield of the dinitro product from 23.5 per cent to 28 per cent of the theoretical, only the meta derivative being obtained. In a second, the use of $(\text{SO}_2\text{OSO}_2\text{ONO}_2)_2$ as a nitrating agent was studied. The authors, Pictet and Karl (163), state that an intermediate addition compound was observed which led only to the *m*-dinitrobenzene. This second investigation suggests a possible reaction scheme involving a molecular rearrangement. The last study to be mentioned concerning nitration is that made by Adkins (1), who found that the action of nitrogen pentoxide on nitrobenzene leads exclusively to the *m*-dinitrobenzene. Further study should be devoted to this case, since information concerning the exclusive formation of a single isomer should be of great importance in solving this problem.

The sulfonation of nitrobenzene has been well nigh completely neglected except for a few workers. Of these, Limpricht (135) has shown that all three isomeric nitrobenzenesulfonic acids are formed when nitrobenzene is treated with fuming sulfuric acid. Though he determined their relative amounts, they were left unidentified except as nitrobenzenesulfonic acids. Nevertheless, Ekbon (56), in a paper on this subject, states that Limpricht obtained about 95 per cent of the meta acid, around 5 per cent of the ortho acid, and the para acid evidently to a very slight degree. This question, however, has been very satisfactorily investigated by Obermiller (155). Sulfonating with sulfuric acid (100 per cent) together with oleum (20 per cent sulfur trioxide) for 2 hours at temperatures up to 60–70°C., he obtained a total yield of 98.3 per cent, of which 98.4 per cent was the meta acid and only 1.6 per cent the para acid. Even by a careful search Obermiller was unable to detect any of the ortho acid among the products. Recalling however the case of benzoic acid, in which the absence of the ortho acid was caused by a molecular rearrangement, and looking forward to other similar cases of sulfonation, it is quite probable that the same is true here also. Generally, therefore, though the case of nitrobenzene apparently contradicts the conception that substitution occurs normally at all three positions, it is quite possible that the absence of ortho substitution on halogenation and sulfonation is the result rather of unusual and specific reaction conditions.

THE SULFO SUBSTITUENT: BENZENESULFONIC ACID

The introduction of a second substituent into the nucleus of benzenesulfonic acid appears to be fairly unsettled. Even in the simple case of halogenation, a hint of the difficulties is provided. Thus, Fittig (61), following up the earlier work of Garrick (72), who heated the sulfonic acid with bromine in a sealed tube but failed to identify an isomer other than the meta, states that the yield consists largely of the *o*- and somewhat of the *p*-monobromosulfonic acids. But Limpricht (136) obtained a satisfactory yield of the meta acid together with some by-products. He treated, however, the silver salt of the sulfonic acid. Though these results are conflicting, the earlier ones may possibly be discarded as unreliable.

The evidence for the nitration of benzenesulfonic acid is chiefly the result of Obermiller's work (155), though Limpricht (135) does report a yield

TABLE 4
The nitration of benzenesulfonic acid

EXPERIMENT NO.	ACTUAL PER CENT OF ISOMERS			PER CENT OF THEORY	RELATIVE PER CENT OF ISOMERS			TOTAL
	Meta	Ortho	Para		Meta	Ortho	Para	
I	68.3	19.9	6.2	94.4	72.4	21.1	6.5	100.0
II	56.4	24.3	9.2	89.9	62.8	27.0	10.2	100.0
III	55.7	23.8	8.7	88.2	63.2	27.0	9.8	100.0
IV	53.6	26.9	11.5	92.0	58.2	29.3	12.5	100.0
V	40.0	27.4	12.2	79.6	50.3	34.3	15.3	100.0

- I. Nitration with 80 per cent nitric acid, but with previous addition of concentrated sulfuric acid, at 20–30°C.
- II. Nitration with 80 per cent nitric acid, without addition of sulfuric acid, at 20–30°C., finally at 50–60°C.
- III. Nitration with 80 per cent nitric acid at 30–40°C., finally at 40–50°C.
- IV. Nitration with 80 per cent nitric acid at 90–100°C.
- V. Nitration with 80 per cent nitric acid at 150–60°C.

consisting of 90 per cent of one isomer and 10 per cent of a second and third together. The results obtained by Obermiller are presented in table 4. It is readily observed that all three isomers are simultaneously formed and that though meta substitution predominates, it is accompanied principally by ortho and to a smaller degree by para substitution. Also the effect of rising temperature substantiates well what has been indicated previously as the usual phenomenon. Furthermore, it must be noted that considerable amounts of the para isomer may be formed under certain conditions. Another most interesting point, recalling Obermiller's work on the sulfonation of nitrobenzene, is that whereas the nitration of benzenesulfonic acid and the sulfonation of nitrobenzene may hypothetically lead

to the same results, the actual yields differ not merely in the relative proportions of the isomers but in the total absence of the ortho isomer in the latter of the two reactions. But inasmuch as in the former reaction there

TABLE 5
Sulfonation of benzenesulfonic acid

DURATION OF HEATING	AT 183°C.	AT 209°C.	AT 233°C.
I. Sulfonations in medium containing free sulfur trioxide			
<i>hours</i>			
4	(mono)	2.0 per cent para	4.7 per cent para
6	---	(2.3 per cent) para	(trisulfo)
12	---	3.0 per cent para	(trisulfo)
18	---	3.0 per cent para	(trisulfo)
24	6.1 per cent para	7.0 per cent para	(trisulfo)
30	---	6.1 per cent para	(trisulfo)
II. Sulfonations with concentrated sulfuric acid (98 per cent)			
3	---	---	11.2 per cent para
4	---	11.1 per cent para	---
6	(mono)	(10.0 per cent) (10.2 per cent) para	12.9 per cent para
12	(mono)	---	19.9 per cent para
18	(mono)	13.7 per cent para	---
24	(mono)	16.1 per cent para	22.0 per cent para
30	---	15.1 per cent para	---
48	14.6 per cent para	22.7 per cent para	28 per cent para
96	---	(trisulfo)	(trisulfo)
168	31.6 per cent para	(trisulfo)	(trisulfo)
III. Transformation of meta acid → para acid at 209°C.			
12 hours heating.....			5.8 per cent para
24 hours heating.....			9.5 per cent para
IV. Transformation of para acid → meta acid at 209°C.			
12 hours heating.....			6.9 per cent meta
24 hours heating.....			11.0 per cent meta
168 hours heating.....			67.0 per cent meta (trisulfo)

is a normal temperature influence, and since in the latter there is a distinct possibility of a molecular rearrangement and an abnormal temperature effect, two distinct mechanisms of benzene substitution are presumably involved. This question will receive further attention below.

The orienting influence of the sulfo group in the formation of benzenedisulfonic acid was a decidedly unanswered question until Holleman and Polak undertook its investigation. Indeed Holleman (reference 98, p. 76) has shown how contradictory was the evidence previous to this time. Although the earlier workers indicate in each case that no ortho isomer is formed, no conclusion can be reached from their results as to whether the para or the meta isomer predominates. The evidence given by Holleman and Polak (110), however, offers a most interesting insight into the question. They studied the effect of temperature, strength of acid, and duration of heating on the one hand and, on the other, the transformation of the para into the meta acid and vice versa. Their results are presented in table 5.

By their work Holleman and Polak have sustained the report that no ortho acid occurs and that the meta isomer predominates. In sections I and II of table 5 they show how the proportion of the para isomer is affected by duration of heating, rise in temperature, and water content of acid reagent. The use of sulfuric acid containing considerable free sulfur trioxide made possible the sulfonation in total absence of water, whereas the use of sulfuric acid (98 per cent) involved the presence of water from the start. A considerably larger proportion of the para acid is formed in the latter case. Furthermore, both higher temperatures and longer heating seem to favor formation of the para acid. To show that this increase of the para acid was caused by a transformation of the meta acid, they treated pure *m*-benzenedisulfonic acid with sulfuric acid (98 per cent) at 209°C. Their results are given in section III of table 5. By comparison with figures in section II, the per cent conversion is seen to be insufficient to account for the formation of the para acid under similar conditions. On the other hand, their results, as in section IV of table 5, show that the transformation of the para acid into the meta acid proceeds to a greater degree, and it is thus seen that for a heating period of 168 hours, the 67 per cent conversion could practically account for the amount of meta acid formed by sulfonation of the monosulfonic acid under like conditions. On the other hand, an examination of section I of table 5 shows that the para acid formed by treatment with oleum could easily be accounted for by conversion of the meta acid into the para acid. Inasmuch as the effect of higher temperatures is to favor para at the expense of meta substitution, and since this is also the case in the sulfonation of benzoic acid, it seems possible that these reactions may follow a similar course. If so, it is important to determine whether or not ortho substitution occurs first, followed by a complete rearrangement to the meta acid. In common with the sulfonation of nitrobenzene and benzoic acid, the sulfonation of benzenedisulfonic acid does not lead ultimately to the ortho isomer. Also these

reactions, it is to be noted, may be contrasted with halogenation and nitration not only by the occurrence of rearrangements but also by the fact that higher temperatures do not favor ortho but rather meta or para substitution.

THE METHYL SUBSTITUENT: TOLUENE

The orienting influence of the methyl group is studied by the introduction of substituents into the ring of toluene. Thus the halogenation of toluene has been very extensively investigated. Indeed the amount of information available is so great and varied that it is difficult at first to draw any conclusions. To make possible, therefore, a better understanding of the experimental data, a few points may first be emphasized. It is immediately recognized that substitution in the methyl group or side chain occurs simultaneously with that in the ring, though special conditions may partially or completely suppress one or the other reaction. In this respect attention should be given to the effect of light, heat, catalysts, and in some measure to the concentrations of the reactants. Consideration of these factors will help to bring order out of apparent chaos. The experimental evidence follows, given in a very brief manner, owing to the unfortunate lack of space.

Glinzer and Fittig (79), by bromination of an excess of toluene in the dark and at ordinary temperatures, obtained a mixture of the *o*- and *p*-bromotoluenes. Similar results were obtained by Huebner and Majert (118), although they chlorinated boiling toluene with gaseous chlorine in the presence of iodine. The use of gaseous chlorine once again, although at water bath temperature and with molybdenum pentachloride as a catalyst, leads principally to *p*-chlorotoluene, some *m*- and probably some *o*-chlorotoluene, according to Aronheim and Dietrich (7). With a method similar to that of Heubner and Majert, Michael and Norton (145) showed that the action of iodine chloride led to *p*-iodotoluene. The effect of temperatures from 97–113°C. and of the presence of iodine was well investigated by Jackson and Field (122), who concluded that high and low temperatures favor side chain and ring substitution, respectively, benzyl bromide becoming the principal product at the boiling point of toluene (111°C.), and that 10 per cent or more iodine is necessary to prevent formation of benzyl bromide at this temperature.

The effect of light was early studied by Schramm (179), who showed that in both chlorination and bromination with iodine present, the ortho and para isomers occurred in both the presence and absence of light. Exposure to light, however, when iodine is not used, effects substitution in the side chain exclusively. According to Schramm, 2 per cent of iodine is sufficient to nullify the influence of light. Somewhat later Seelig (182)

confirmed the finding that chlorination at the boiling point led largely to side chain substitution, and in addition showed that the presence of iodine, molybdenum pentachloride, and ferric chloride induces nevertheless a predominant yield of the para and in any case some of the ortho isomer. Chlorination of an ice-cold mixture was found by Seelig to provide as much as 65 per cent of *o*-chlorotoluene and as little as 25 per cent of *p*-chlorotoluene. The work of this investigator indicates that when in the absence of a catalyst side chain substitution is at a minimum, ortho substitution prevails over para substitution. Pointing out the fact that Beilstein and Geitner (22) had obtained on chlorination the ortho isomer as the main product, this evidence strongly suggested the possible ortho orienting nature of the methyl substituent.

Using sulfuryl chloride as a reagent, Toehl and Eberhard (199) obtained at 160°C. one-third of their product as benzyl chloride and two-thirds as a mixture of *p*-chlorotoluene and the 3,4-dichlorotoluene. Edinger and Goldberg (55) used sulfuryl bromide together with nitric acid (1.4) and benzene as a solvent. A mixture of *p*- and *o*-bromotoluene amounting to 85 to 95 per cent was obtained. Iodinating in the same fashion (54) they obtained the corresponding iodo derivatives amounting to 60 to 70 per cent of the theoretical quantity. O. Silberrad (187) and his coworkers have also used sulfuryl chloride, but in conjunction with a variety of catalysts. Chlorinating at 70°C. with aluminum chloride and 1 per cent sulfur chloride in the reagent, Silberrad obtained 88 per cent of a mixture of *o*- and *p*-chlorotoluenes in the approximate proportion of 1:1.3, respectively. In another report (186) they state that the use of phosphorus pentachloride, manganous chloride, or arsenic acted to prevent ring substitution and to favor formation of benzyl chloride. The reactions were carried out with boiling toluene. The use of sulfuryl chloride in place of chlorine apparently permits ring substitution even at a high temperature. Catalysts generally favor ring substitution, but it is of significance that some actually aid the formation of benzyl chloride.

Though Seelig found that ferric chloride as a catalyst favored para substitution, Thomas (195) used it as a reagent with boiling toluene to give a mixture of chlorotoluenes and no benzyl chloride. Cohen and Dakin (38), using an aluminum-mercury couple and chlorinating with chlorine, presumably at room temperature, obtained 65 per cent of the ortho and 35 per cent of the para isomer from a total yield of 80 per cent of the theoretical. Chlorinating with ammonium plumbic chloride, Seyewitz and Biot (184) obtained *o*-chlorotoluene. Whereas ferric chloride seems to favor para substitution, ammonium plumbic chloride effects ortho substitution.

The question of side chain versus ring substitution was reopened by the study of Cohen, Dawson, and Crossland (39) on the action of electrolytic

chlorine. By comparative studies between chlorine from pyrolusite and hydrochloric acid and electrolytic chlorine from carbon electrodes and hydrochloric acid and the presence of carbon, they determined that even with boiling toluene, electrolytic chlorine attacked only the ring. Extending these studies, Schleuderberg (178), using platinum electrodes in diffused light, showed that at the temperature of melting ice and at current densities above 1.3 ampere hours side chain substitution occurred appreciably. His findings were as follows: (1) Lower current density favors ring substitution and total efficiency. (2) Electrolytic chlorine will substitute in the side chain of boiling toluene. (3) Chlorine obtained from unstable compounds such as plumbic chloride and ferric chloride substitutes in the ring. Further work by Cohen, Dawson, and associates (40) has confirmed the fact that benzyl chloride is formed even at low current densities and in the dark. For an average they obtained 10 per cent benzyl chloride and 90 per cent *o*- and *p*-chlorotoluenes. Similar experiments, though in the presence of light, gave 64 per cent side chain and 36 per cent ring substitution. Investigation of the effect of moisture indicated an 8 to 9 per cent shift in favor of ring substitution. Another electrolytic study was made by Fichter and Glanzstein (60) who, using a glacial acetic acid medium and darkness, obtained the para and ortho isomers in the ratio 2.5:1. But they report Muehlhofer as having found more of the ortho isomer. Generally the work on electrolytic chlorination indicates that ring and specifically para substitution are thereby favored. At the same time high temperatures and light appear as stronger factors in aid of side chain substitution. The findings of Cohen and coworkers to the contrary do not appear to be completely confirmed by later work. Electrolytic chlorine nevertheless fills a rôle very similar to catalysts.

The effect of catalysts as well as temperature and light has been the subject of an excellent study by Van der Laan (200). Results of bromination with bromine show that both with and without catalysts, temperature is a dominant factor in the formation of benzyl bromide. Without a catalyst, a temperature of 50°C. causes about equal amounts of side chain and ring substitution, while at 100°C. no ring substitution occurs at all. The presence of antimony bromide at 50°C. and above has practically no effect. The effect of light is well defined, however, for without a catalyst at 30°C. there is 99 per cent side chain substitution, whereas with catalysts such as antimony bromide, aluminum bromide, or ferric bromide, there results a mixture of polybromotoluenes and no benzyl bromide. Here it seems that catalysts exert a stronger influence than light. Van der Laan's experiments in darkness with so-called bromine carriers showed that even with increasing amounts of antimony bromide there always remain appreciable amounts of benzyl bromide. On the other hand, comparatively

small quantities of aluminum bromide or ferric bromide will prevent side chain substitution completely. Adding aluminum in an aluminum-mercury couple instead of the free metal apparently has no effect. The figures for phosphorus, however, indicate a catalyst favoring side chain substitution, without effect on the ortho-para ratio. But it should be pointed out that this ratio is affected by the other catalysts studied. Presence of antimony bromide or ferric bromide decreases the proportion of ortho to para, whereas aluminum bromide acts in the opposite way. Change of the ortho-para ratio with temperature is quite well defined. Both ortho and side chain substitution are favored by rise in temperature. Generally it may be said that Van der Laan's work demonstrates well the specific effect of such factors as temperature, light, and catalysts with regard to bromination.

Using the same reaction Holleman and Polak (109) have studied the influence of concentrations of reactants and found that as the proportion of toluene to bromine increases, side chain substitution occurs to a greater degree, an effect which is greatly augmented by higher temperatures. Their work also indicates that only at 50°C. is there any appreciable effect on the ortho-para ratio, more ortho substitution occurring at lower concentrations of bromine. It appears, therefore, that an increase in temperature and a decrease in concentration of bromine augments both ortho and side chain substitution.

An interesting review of this problem has been made by Bancroft (19). Drawing on the work of others as well as on his own he summarized the situation concerning bromination and chlorination as follows:

Toluene and bromine:

Ring and chain substitution in the dark; concentration and temperature effect.

Ring and chain substitution with bromine and water.

Chain substitution in sunlight.

Chiefly chain substitution in sunlight in presence of nitrobenzene.

Chiefly ring substitution in the dark in presence of nitrobenzene.

Ring substitution with ferric bromide, ferric chloride, etc.; concentration effect.

Ring (and chain) substitution with iodine bromide; concentration and temperature effect.

Toluene and chlorine:

Ring and chain substitution in the dark; temperature effect.

Chain and some ring substitution in the dark with water or dilute sodium hydroxide.

Chain substitution in the daylight.

Ring substitution with ferric chloride, iodine chloride, antimony pentachloride, etc.

Ring substitution by electrolysis.

Chain substitution with sulfur as a carrier.

Chain substitution with phosphorus pentachloride.

One can see here how closely alike are bromination and chlorination, enough so in any case to consider them together. Of special interest is the fact that the presence of sulfur and phosphorus pentachloride favors chain substitution. It has already been mentioned that Silberrad found phosphorus pentachloride to act in this way and in addition Andrich and Le Blanc (3) have found oxygen to exert a similar influence in the bromination reaction. Indeed it might be well at this point to recall the close relationship of oxygen, sulfur, and even phosphorus.

Although chain substitution may be hindered by darkness and low temperatures, certain types of solvents or reaction mediums have the same effect. Bruner and Vorbrodt (30a) found bromination of toluene in the side chain to be less than 0.86 per cent whether in darkness or light when the reaction was carried out in the following solvents: carbon bisulfide, carbon tetrachloride, benzene, chloroform, acetic acid, phenylcyanide, nitrobenzene. Not only this point but the variation in effectiveness of the solvents suggests the importance of the reaction medium. The work of Elbs and Jaroslawzew (57) is also of interest in this respect. They treated toluene and iodine dissolved in glacial acetic acid with sodium persulfate. Their yield amounted to 86 per cent and consisted mainly of *o*- with some *p*-iodotoluene. It would appear here, however, that perhaps the salt rather than the solvent exerted the greater influence.

An acid medium was employed by Datta and Fernandes (48), who chlorinated toluene in aqua regia. Using nitric and hydrochloric acids in the ratio 1:1, they obtained principally benzyl chloride and considerable *o*-chlorotoluene. But with a ratio of 2 HCl:1 HNO₃ the formation of benzyl chloride scarcely occurred at all, while ortho substitution prevailed together with some para substitution. The reactions were carried out at water bath temperature. It should be noticed that chain and ortho substitution occur together under the first conditions and that when the former is suppressed, para substitution begins to occur at the same time that ortho substitution predominates. A similarity between chain and ortho substitution is surely suggested, as well as the ortho orienting nature of the methyl substituent.

Ortho substitution apparently occurs to a greater extent in the case of bromination also, as shown by Datta and Chatterjee (45). Using nitric acid (1.35) and bromine they obtained a 40 per cent yield of *o*-bromotoluene and some 3,4-dibromotoluene. Iodination in the same way gave merely a mixture of the para and ortho isomers (46). No benzyl bromide apparently was obtained by Stark (190), who also used an acid medium. Bromination

with hypobromous acid gave him a 73 per cent yield consisting of a mixture of the ortho and para isomers.

Another investigation to be mentioned here is that of Wahl, Normand, and Vermeylen (205). Chlorinating in the presence of iron and at 30–60°C., they obtained 57.8 per cent of *o*-chlorotoluene. With ammonium plumbic chloride, as reported by Seyewitz and Biot (184), they could obtain no reaction. The use, however, of plumbous chloride at 700°C. gave them 62 per cent of the ortho and 38 per cent of the para isomer. Comparing the result of the iron catalyst reaction with the studies of Aronheim and Dietrich (7), Thomas (195) and Seelig (182), all of whom used ferric chloride, it appears that they obtained an unusual yield of the ortho isomer. The contradictory nature of Van der Laan's work (200) should also be recalled. Chlorination with plumbous chloride appears unusual in the same way with a predominance of ortho substitution. However at 700°C. it would be difficult to predict results. Higher temperatures generally favor ortho substitution, yet it is also known that under such conditions substituents are likely to change positions in the ring.

Before concluding the discussion of halogenation of toluene a few general remarks should be made. Temperature plays such a rôle that heat favors ortho as well as chain substitution, whereas cold aids in ring and specifically in para substitution. Light definitely aids chain and hinders ring substitution. Its effect on the ortho–para ratio would be of interest could it be successfully determined. With respect to concentration of reactants, it may be said that an excess of toluene is in favor of chain and possibly ortho substitution. The situation with regard to catalysts and reagents other than the pure halogens is scarcely so well defined. Superficially the most effective ones are those leading to para substitution, such as antimony trichloride, molybdenum pentachloride, iodine, ferric chloride, etc. Inasmuch as they simultaneously further ring substitution, the most abundant and exact data concerns them and consequently shows the methyl group as a para orienting substituent.

Turning now to the other type of catalyst, that favoring ortho substitution, there appear to be several. Recalling Seelig's work, that of Datta and Fernandes, Cohen and Dakin, and similarly the investigation of Wahl, Normand, and Vermeylen, it appears not infrequently that ortho substitution predominates. As will be evident throughout this paper, high temperatures favor ortho substitution generally just as in this case, but with chain substitution possible and favored by the same circumstance, it is probable that much chain substitution occurs in place of ortho substitution. For this reason, and because of the fact that ortho substitution does frequently constitute the major reaction, it is well to consider the possibility

of the methyl group as an ortho orienting substituent. Furthermore, as has been indicated here and there, certain conditions and catalysts favor either chain and ortho substitution or ring and para substitution. Indecisive as the evidence may be as to whether toluene effects largely ortho or para substitution, considerable support is given to this view from studies on nitration.

Concerning the nitration of toluene a discussion of evidence will be reserved until the experimental work has been presented. Thus Rosenstiehl (172) has nitrated toluene with nitric acid (1.475) and indicates that the main product is *o*-nitrotoluene with half as much of the para isomer. Monnet, Reverdin, and Noelting (146) have shown that the meta isomer occurs simultaneously, though in almost negligible amounts, together with the ortho and para isomers. Leeds (134) nitrated toluene with nitrogen peroxide and obtained, besides polynitrated products, principally if not exclusively *o*-nitrotoluene. Noelting and Forel (153) state that nitration of toluene with nitric acid alone gives a preponderant yield of the para isomer (ca. 66 per cent), whereas nitration with a nitric and sulfuric acid mixture gives the same yield of the ortho isomer. They found the reaction temperature and concentration of acids to exert an influence on the ratio of isomers. Welter (206) has demonstrated the effect of temperature, obtaining, at 30–35°C., 60 per cent of the ortho and 40 per cent of the para isomer; at 50–55°C., 85 per cent of the ortho and 15 per cent of the para isomer. Holdermann (95) investigated the effect of catalysts on the nitration reaction when nitric acid was used both alone and together with sulfuric acid. Experimenting with copper, copper nitrate, mercury, mercurous nitrate, mercuric sulfate, nickel, cobalt nitrate, and ammonium vanadate at 5–10°C., he found the yield of ortho isomer to vary but negligibly from that obtained without a catalyst, namely 59 to 60 per cent. The use of nitric acid (1.52) alone gave 52.6 to 52.7 per cent of the ortho isomer and similar results in the presence of catalysts. Orton (159) nitrated toluene using nitric acid (94 to 95 per cent) of 1.3 to 1.4 per cent nitrous acid content. A mixture of the ortho and para isomers amounting to 17 to 18 per cent of the theory resulted. A quantitative yield, however, was obtained by employing a glacial acetic acid medium. Pictet and Khotinsky (164) treated toluene with acetyl nitrate, securing 88 per cent of the *o*-nitro and 12 per cent of the *p*-nitro derivative. Boedtker (27) nitrated toluene at water bath temperature with ethyl nitrate, adding aluminum chloride to the reaction mixture little by little. The yield consisted of 20 g. of the ortho and 4 g. of the para isomer. According to Friswell (69) nitration of toluene always gives 60 to 65 per cent of the ortho and 35 to 40 per cent of the para isomer.

Concerning the influence of temperature, Holleman and van den Arend

(112) made an excellent study, nitrating with nitric acid (1.475). Repetition of this work several years later by Holleman and coworkers (114) gave presumably more accurate results. Their results are given in table 6. Kidokoro (130) investigated this problem but his results add little except to show that the presence of sulfuric acid favors the para isomer, raising it from 45 per cent to 60 per cent, the balance being apparently the ortho isomer.

Davis, Worral, Drake, Helmkamp, and Young (49) investigated the effect of mercuric oxide. Using 10 g. of mercuric oxide to 200 g. of toluene, they obtained results which indicate substitution to take place about equally in the ortho and para positions. Gibson, Duckham, and Fairbairn (77) nitrated with strong nitric acid and with mixed sulfuric and nitric acids in various proportions. The effect of temperature and their determination of the meta isomer are the most satisfactory parts of their work. Though rise in temperature increases ortho substitution but slightly, the

TABLE 6
Nitration of toluene with nitric acid (1.475)

TEMPERATURE	NITROTOLUENES		
	Ortho	Meta	Para
<i>degrees C.</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
-30	57.2	3.5	39.3
0	58.0	3.9	38.1
30	58.8	4.4	36.8
60	59.6	5.1	35.3

persistence of this effect throughout three series of experiments makes it convincing. On account of the variable quantities of reactants and the slight change in the ratio of isomers, no other conclusions can be drawn, although it is obvious that substitution does occur in all three positions.

Of peculiar interest is the work of Menke (142). The exclusive preparation of *o*-nitrotoluene by nitration with ferric nitrate in acetic anhydride solution is certainly unique, for no case of this kind has yet been mentioned. It will be recalled how para is generally supposed to accompany ortho substitution. However from another point of view concerning the relation of the isomeric positions this is not an unusual circumstance, for meta substitution likewise frequently occurs practically alone. Haines and Adkins (88) have nitrated with nitrogen pentoxide in a carbon tetrachloride medium, but the boiling point (228°C.) of their product gives no information as to its composition.

Reviewing the experimental evidence now, it is apparent that either ortho or para substitution may prevail. The latter type, however, appears

as a more special case, particularly in view of the excellent studies of Holleman and coworkers and of Gibson, Duckham, and Fairbairn. Their work definitely marks the preponderance of ortho substitution. In addition, one will readily realize that the ratio of isomers depends not merely on the nature of the methyl substituent but also on the reagent, concentration of reactants, reaction medium, temperature, and catalysts. But it is only concerning the temperature that any inferences can be made. Thus, rising temperature increases the yield of the ortho isomer and decreases that of the para isomer. Higher temperatures also favor meta substitution, which fact should not be neglected. Indeed the occurrence of the meta isomer and the above temperature effect marks this reaction as taking place in the manner previously described as the normal one. Finally it should be emphasized that the ortho orienting nature of the methyl substituent receives considerable support from the above evidence.

Concerning the case of sulfonation, it will be seen that on account of the occurrence of molecular rearrangements the facts are rather confusing. Nevertheless, the very thorough work of Holleman and Caland (104) is quite satisfactory. Considerable study had previously been devoted to this problem, but no decisive results had been obtained. Inasmuch as this earlier work offers nothing of special interest, attention will be given directly to that of Holleman and his coworker. Their study included the effect of temperature, the concentration of the sulfuric acid, the ratio of toluene to acid, and the presence of salts. In addition, they compared sulfuric acid with chlorosulfonic acid as sulfonating agent and investigated the transformation of the isomeric toluenesulfonic acids into one another. It was also of importance that they proved the simultaneous formation of the meta together with the para and the ortho isomers. This had previously been a much disputed question.

Of least interest perhaps is their study of sulfonation in the presence of salts. They used potassium sulfate, mercurous sulfate, and silver sulfate, and determined that they did not appreciably affect the proportion of isomers. From their other studies, however, it may be readily observed that meta substitution always occurs, varying from 2.5 per cent under certain conditions up to 14.4 per cent under other conditions. In the latter case the amount of meta substitution exceeds that of ortho by 10.7 per cent, para substitution occurring to the extent of 81.7 per cent. By comparison with the other results, this particular case was apparently due principally to the high temperature of 100°C. and partially to the small ratio of toluene to acid, namely 1:41.5. This is somewhat contrary to the conception that para and ortho substitution are always associated together, for in that case meta substitution should not occur at all.

Now although no conclusions regarding the effect of acid strength and

sulfuric acid (1.84) and a trace of iodine. After one hour at 100°C. they obtained the para acid exclusively in a 90 to 95 per cent yield. Gebler (76) similarly obtained an 87 per cent yield of the para acid by heating one part of toluene with 2.5 parts of trihydrogen sodium sulfate, $\text{NaH}_3(\text{SO}_4)_2$, under a reflux condenser for fifteen to sixteen hours. Nevertheless, these are both special methods of sulfonation and do not invalidate the idea that the sulfo group is mainly introduced in the ortho position and that the final product is caused by a molecular rearrangement of a large part of the ortho acid. Concerning the work of Ray and Day it is not surprising that sulfonation at 100°C. and in the presence of iodine led only to the para acid, for high temperatures favor the rearrangement and iodine is generally a catalyst favoring para substitution.

Generally the sulfonation of toluene is seen to be a case where the true orienting influence is hidden by a molecular rearrangement. At the same time one can readily infer the ortho orienting nature of the methyl substituent, which would confirm the findings with regard to halogenation and nitration. Though this point of view can hardly be insisted upon at present, the methyl substituent does appear to be more nearly ortho orienting than any other.

THE HYDROXYL SUBSTITUENT: PHENOL

The methods used in the halogenation of phenol may be divided conveniently into two groups according to whether or not a solvent is used, although apparently the reaction is quite satisfactory either way. Thus Dubois (51) chlorinated with sulfuryl chloride and obtained a monochlorophenol which was identified as the para isomer. Using chlorine gas with cooling, the same worker (52) obtained a mixture of monochlorophenols of which it could only be inferred that the major part was the para isomer. On the other hand a preponderant yield of the ortho isomer was identified as such by Faust and Mueller (59). They treated liquid phenol with chlorine, a method later used by Hasse (91), whose results do not confirm those of Faust and Mueller. That the higher temperature (41°C.) necessary for liquid phenol may have caused a main yield of the ortho isomer is substantiated by a patent belonging to Merck in Darmstadt (143). This patent claims an almost exclusive yield of the ortho isomer by treatment of phenol at 150–180°C. with either chlorine or bromine. This claim is confirmed by a similar investigation of Bramley (30), although he did obtain also the para isomer, together with a little dichlorophenol. Concerning chlorination, supposedly at room temperature, the Jahresbericht (124) describes *o*-chlorophenol as the by-product and *p*-chlorophenol as the main product. The same case is stated for bromination and iodination with iodine and iodic acid. With regard to this, Varnholt (204) has re-

ported that chlorination of phenol under cooling leads to a mixture of *o*- and *p*-chlorophenols, of which 30 per cent is the ortho isomer. From the above work it appears that on chlorination at ca. 180°C., the ortho isomer forms the major product, while at ca. 0°C. the para isomer predominates. It is of interest then that at 90°C. Holleman (99) obtained equal yields of *o*- and *p*-chlorophenols (49.8 per cent ortho, 50.2 per cent para). Bromination at the same temperature, however, according to Holleman gives 9.3 per cent of *o*- and 90.7 per cent of *p*-bromophenol. Though rising temperature favors ortho substitution in both chlorination and bromination, according to Holleman and Rinkes (111) at 180°C. the *p*-bromophenol still amounted to 77 per cent of the yield. With regard to chlorination, they state that temperature similarly has but slight effect and that the per cent of ortho isomer is little higher than in bromination. In no case could they detect the meta isomer.

In the same investigation, Holleman and Rinkes studied the effect of carbon disulfide, glacial acetic acid, and carbon tetrachloride when used as solvents. Bromination at temperatures from -30°C. to 30°C. gave preponderant yields of para with the balance as the ortho and none of the meta isomer. Use had been made previously of carbon tetrachloride at low temperatures by Lossen (138), who in this way obtained only the *o*-chlorophenol. Gomberg and Stone (83) used the same method to prepare the *o*-chlorophenol, but their work merely indicates that more ortho isomer is thus obtained than by direct chlorination. Baines (11) also used carbon tetrachloride as a reaction medium for bromination, but he did not determine whether the ortho or the para isomer was in excess. Nevertheless, for chlorination carbon tetrachloride seems to favor ortho substitution. With regard to bromination, Hantzsch and Mai (89) report that a dilute carbon disulfide solution yields the pure para isomer up to 85 per cent of the theoretical. This result is in good agreement with that of Holleman and Rinkes. Similarly, work by Huebner and Brenken (117) and by Meldola and Streatfield (141) with respect to the use of glacial acetic acid offers quite analogous results.

Halogenation in alkaline mediums, on the other hand, gives unusual results. Both Chandon (33) and Skraup and Beifuss (188) obtained in this way more of the ortho than of the para isomer. Indeed, by chlorination with sodium hypochlorite in a caustic potash solution, Chandon obtained in addition to dichlorophenol, only the *o*-chlorophenol. Skraup and Beifuss found that bromination in pyridine or in an aqueous alkaline solution, such as sodium hypobromite, at room temperatures gave up to 54 to 64 per cent of *o*-bromophenol together with small amounts of di- and tri-bromophenols. On the other hand, Tishchenko (198) treated an aqueous solution of phenol with a concentrated solution of sodium carbonate con-

taining one equivalent of bromine and reported a yield of over 70 per cent *p*-bromophenol. In analogous experiments, using chlorine in place of bromine, equal quantities of both *o*- and *p*-chlorophenol were obtained. On the whole, it appears that an alkaline solution actually favors ortho substitution. In this respect it is interesting to recall a similar situation in the case of halogenation of benzoic acid.

In summarizing the evidence on halogenation it can be said that bromination occurs too strongly at the para position to be much affected by temperature or the reaction medium. Chlorination, however, varies considerably, ortho substitution being favored by higher temperatures, by the use of carbon tetrachloride, and by an alkaline reaction medium. Otherwise para substitution occurs to a greater degree than ortho substitution. Although the temperature effect corresponds to what has been considered normal, the absence of the meta isomer appears as unusual. With respect to nitration, however, it is seen that substitution readily occurs in all three positions.

From all the evidence available the nitration of phenol leads generally to more *o*- than *p*-nitrophenol. This is indicated by the very early work of Fritzche (70) and is definitely stated by Gatterman (74). Nitration with a mixture of sodium nitrate and sulfuric acid in aqueous solution at 20–25°C. will give 30 g. of the ortho and 5 to 10 g. of the para isomer. It might also be mentioned here that, according to Holleman (98, p. 164), gradual addition of dilute nitric acid to phenol will favor nitration in the ortho position. But the most recent study shows practically equal yields of the two isomers. Thus Beaumont and Haemmerle (20), nitrating in water, alcohol, or glacial acetic acid with nitric acid (1.35) at 7–12°C., obtained 77 to 82 per cent yields of nitro compounds. These products consisted of 40 per cent of *o*-nitrophenol, 35 to 40 per cent of *p*-nitrophenol, and 2.5 per cent of 2,4-dinitrophenol. They also found that higher temperatures favored ortho substitution, while lower temperatures favored para substitution, an observation which had been made much earlier by Goldstein (82). The influence of temperature is also very accurately shown in an investigation by Arnall (5). His results are given in table 7. The temperature effect, though not great, is the same as observed by Goldstein. Of greater interest, however, is the fact that Arnall always obtained a definite yield of the meta isomer. That this is not caused by the use of glacial acetic acid is shown by his experiments with a variety of other solvents, including acetone, ether, and alcohol. With all of them approximately the same yield of nitrophenols was obtained. He did find, however, that the total yield of nitrophenols varied from 98.7 per cent in glacial acetic acid to only 55 per cent in absolute alcohol. In addition to showing that nitration occurs in all three positions, Arnall's work confirms

the ortho orienting influence of the hydroxyl group toward an incoming nitro group.

Other methods besides the use of nitric acid generally indicate the preponderance of ortho substitution. Unfortunately Weselsky (207), nitrating in an ether solution with nitrogen trioxide, failed to determine the relative amounts of the ortho and para isomers. But Auwers (9), by treating 1 g. of phenol in a benzene solution with nitrogen peroxide in the cold, secured 0.5 g. of the *o*- and 0.4 g. of the *p*-nitrophenol. On the other hand, Wieland (209) obtained nearly twice as much para as ortho, using the same method except that the solvent was a mixture of benzene and benzine. Natanson (150) nitrated with ethyl nitrate and sulfuric acid at 55°C. and reported 22 per cent of *o*-nitrophenol and 0.5 per cent of *p*-nitrophenol. Francis (65) also reported the ortho isomer to be in excess when he nitrated a carbon tetrachloride solution of phenol with benzoyl nitrate. Pictet (162) used acetyl nitrate in the same way to obtain 52 per cent of the ortho

TABLE 7
Nitration of phenol in glacial acetic acid

PER CENT OF HNO ₃ IN CH ₃ COOH	AT 10°C.			AT 25°C.			AT 45°C.		
	Ortho	Meta	Para	Ortho	Meta	Para	Ortho	Meta	Para
	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
5	57.6	3.3	40.0	58.1	2.9	39.0	59.4	2.4	38.2
10	57.8	3.1	39.1	59.2	2.7	38.1	60.6	2.2	37.2
20	58.9	2.8	38.3	60.3	2.4	37.3	61.5	2.1	36.4

and 48 per cent of the para isomer. Nitration with bismuth nitrate and acetic anhydride, according to Spiegel and Hayman (189), gives the ortho and para isomers in the ratio 2:1.1. Despite, therefore, one or two cases to the contrary, the evidence indicates generally the prevalence of ortho over para substitution. In addition, Arnall's work indicates meta substitution even though its occurrence in halogenation is very doubtful. Finally, nitration appears to occur in the normal fashion, involving all three positions and the usual temperature effect.

The sulfonation of phenol presents a problem very similar to that of toluene. In both cases and also in that of aniline, as will be seen later, a transformation of the ortho into the para isomer hides the true orienting influence of the substituent group. As first shown by Kekulé (129), sulfonation leads to both *o*- and *p*-phenolsulfonic acid. The transformation of the ortho into the para isomer was investigated by Post (166), who showed that long heating, high temperatures, and stronger sulfuric acid were favorable to this conversion. Schultz and Ichenhauser (180) have con-

firmed the work of Post by showing that long heating leads largely to the para isomer. Obermiller (154), sulfonating at 20°C. with 100 per cent sulfuric acid, obtained about two parts of the ortho to three parts of the para acid. He found lower temperatures and weaker acids to favor ortho substitution. More recently Margueyrol and Loriette (140) have prepared the para acid by treating phenol with sulfuric acid (94.5 per cent) for five to six hours at 125–130°C.

Now although none of the above workers reports the formation of any *m*-phenolsulfonic acid, there is reason to believe that some meta substitution does occur. Salomonoff (174) sulfonated phenol for a period of several days at room temperature and reported the formation of a very small quantity of a third isomer. Though recognizing the possibility that this may be phenylsulfuric acid, Holleman (98, p. 166) states that the meta acid may be among the reaction products, inasmuch as fusion with caustic potash gives a little resorcinol. Furthermore it has been shown, according to the same authority, that neither the para nor the ortho isomer, but only the meta acid will in this way give resorcinol.

The phenylsulfuric acid is believed by Holleman (98, p. 170) to be an intermediate product, since this compound is found with the reaction products after sulfonation for 3 hours at 0–5°C. Furthermore, heating the potassium salt of phenylsulfuric acid in a sealed tube at 150–160°C. converts it into the potassium salt of *p*-phenolsulfonic acid. He ascribes the absence of the ortho isomer to high temperature. These experiments certainly suggest a very probable reaction scheme, viz.,



Reference should be made here to a very excellent review of this problem by Olsen and Goldstein (157). They show that the ortho acid increases from less than 5 per cent at 70°C. to over 50 per cent at 20°C. The ortho acid is also shown to vary from 10 per cent when fuming sulfuric acid is used, to nearly 60 per cent for acid between 80 to 85 per cent at a sulfonation temperature of 35–40°C. But of special interest is their statement that the transformation of the ortho into the para acid is true molecular rearrangement.

If now the para acid is formed largely by transformation of the ortho acid, the hydroxyl group appears as an ortho orienting substituent. Both sulfonation and nitration lead therefore to this conclusion. In any case it is important to notice that sulfonation of both phenol and toluene appears to proceed in similar fashion.

THE AMINO SUBSTITUENT: ANILINE

Unfortunately there is not an abundance of evidence concerning the halogenation of aniline. In one of the earliest investigations Kekulé

(128) allowed bromine to react on aniline in a benzene solution and obtained, in addition to dibromo- and tribromo-aniline, *p*-bromoaniline with admixture of almost negligible amounts of either the meta or the ortho isomer or both. Using gaseous bromine mixed with air, exactly similar results were obtained. With regard to chlorination, Holleman (98, p. 138) states that Hafner treated aniline in an excess of either concentrated sulfuric or hydrochloric acid with chlorine and obtained *p*-chloroaniline. Similarly, bromination leads to *p*-bromoaniline. Bromination was also studied by Hoffman (94), who treated aniline with 1.5 times the amount of powdered iodine and obtained, besides hydriodic acid and aniline hydroiodide, *p*-iodoaniline. The para isomer was also obtained by Fuchs (71), who brominated aniline in a glacial acetic acid medium. Elbs and Volk (58) iodinated in concentrated hydrochloric acid with iodine and sodium persulfate. In addition to a main yield of 2,4-diiodoaniline, there resulted a very small amount of *p*-iodoaniline.

All of the above evidence points to a strong para orienting influence. Indeed, the ortho and the meta isomers do not appear to occur at all. Nevertheless, Holleman (98, p. 134) mentions two cases in which considerable ortho substitution occurs. Thus Chattaway and Orton (34) showed that aniline could be chlorinated with acetylchloramidodichlorobenzene. Using chloroform as a reaction medium, they found that *o*- and *p*-chloroaniline were formed in about equal amounts. Of considerable interest also is the fact that Fries (68) was able to obtain crystallized addition products by treating aromatic amines in glacial acetic acid with bromine and hydrogen bromide. The addition of water caused a quick conversion in which the ortho and para derivatives always resulted. This study shows how the formation of an intermediate addition compound may well be the first step in these substitution reactions.

Besides indicating the para orienting nature of the amino group, the above investigations offer very little. It seems highly improbable that para substitution occurs alone and therefore more exact information with regard to the possible extent of ortho and meta substitution is needed. Furthermore no one has investigated the effect of temperature, and, as will appear throughout this paper, the temperature effect becomes an index of the type of substitution reaction involved.

Though the same criticism may be made of the evidence regarding nitration, the situation is nevertheless more satisfactory. The earliest study is that of Huebner (116), who nitrated aniline sulfate with a mixture of fuming sulfuric and nitric acids. His product consisted of more *m*- than *p*-nitroaniline and of a very slight amount of the ortho isomer. This result is confirmed by Bruns (31), whose yield of nitroanilines was 10 to 15 per cent of the ortho isomer, and 45 to 50 per cent of the para and meta isomers

together. Bamberger (14), however, obtained only the ortho and para isomers. His procedure was to treat aniline with nitrogen pentoxide in an ether solution, which easily accounts for his results. For both Huebner and Bruns, by using sulfuric acid, were virtually nitrating aniline sulfate and not aniline. The amino salt substituent is well known as a meta orienting one and inasmuch as Bamberger avoided its presence he did not obtain the meta isomer. Nitrating with nitrogen peroxide, just as with the pentoxide, Bamberger (15) again obtained small amounts of the ortho and para isomers, though principally diazoaminobenzene. Meta substitution again failed to occur when Hoff (93) treated aniline nitrate with acetic anhydride. The *o*- and *p*-nitroanilines were obtained in the ratio of eight to one, in addition to diazo compounds. Here then it seems unusual that no meta isomer resulted, but one must remember that this is probably a case of molecular rearrangement, not of direct nitration of aniline salt. Holleman, Hartogs, and van der Linden (107) have made a somewhat more thorough investigation along the same line, treating aniline nitrate with glacial acetic acid. Their results are as follows:

ANILINE NITRATE	GLACIAL ACETIC ACID	TEMPERATURE	YIELD	NITROANILINES		
				Ortho	Para	Meta
		<i>degrees C.</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
4 g.	40 cc.	0	29.7	82.1	2.9	15.0

Here there is the same preponderant yield of the ortho isomer, but the para and the meta isomers also occur in appreciable amounts, the former to a greater degree than the latter. Proof that this reaction is not the usual type, but in fact a molecular rearrangement, is provided by Holleman and his collaborators. They treated phenylnitroamine with sulfuric acid and secured the results given below:

PHENYL- NITROAMINE	SULFURIC ACID (74 PER CENT)	TEMPERATURE	YIELD	NITROANILINES		
				Ortho	Para	Meta
		<i>degrees C.</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
5 g.	50 cc.	-20	66.1	95	3.5	1.5

Comparison of these results with those above suggests at once that the formation of phenylnitroamine is an intermediate step in the conversion of aniline nitrate to nitroaniline. The function of the glacial acetic acid would appear to be that of a dehydrator, and indeed it may be that acetic anhydride (as in Hoff's experiment) might act so strongly as to prevent meta substitution completely. The same workers have nitrated aniline

with nitric acid in a sulfuric acid medium. They have also treated aniline nitrate with concentrated sulfuric acid, both with and without nitric acid. Their results are given in table 8.

It is strange that so little of the ortho isomer occurs and that the main yield is divided between the meta and para isomers. In comparing these figures with those for conversion of aniline nitrate and phenylnitroamine with acetic acid and sulfuric acid, respectively, it is fairly obvious that in this case a different reaction mechanism is involved. A determination of the temperature influence might also serve to distinguish these two cases. The principal value of this study, however, is in demonstrating the simultaneous formation of all three isomers and the fact that meta substitution does occur so prominently.

TABLE 8
Nitration of aniline at -20°C .

NO.	CC. OF SULFURIC ACID PER GRAM OF ANILINE	NITROANILINES			PER CENT YIELD AT -20°C .
		Ortho	Meta	Para	
		<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	
1	5	1.4	47.9	50.7	75
2a	20	2.1	46.6	51.3	94.5
2b	20	1.0	47.5	51.5	97
3	50	1.3	49.1	49.6	80
4	3 g. of aniline nitrate in 40 cc. of H_2SO_4 (95 per cent)	4.0	39.0	56.0	91
5	3 g. of aniline nitrate in 40 cc. of H_2SO_4 (90 per cent)	4.5	39.5	56.0	92
6	2 g. of aniline nitrate in 40 cc. of H_2SO_4 (80 per cent) 20 cc. HNO_3	5.0	32.0	62.0	91

Other investigators, using a variety of nitrating agents, have generally obtained more of the ortho than of the para and none of the meta isomer. This was the case with Witt and Utermann (210), who used a mixture of nitric acid and either acetic anhydride or glacial acetic acid. Both Francis (65), using benzoyl nitrate in carbon tetrachloride, and Pictet (162), using acetyl nitrate in dilute carbon tetrachloride or acetic anhydride, obtained the ortho derivative exclusively. It must be mentioned however that all these investigations were made with acetanilide. Notwithstanding this, Menke (142) did obtain the pure ortho isomer from aniline by nitration with cupric nitrate trihydrate in an acetic anhydride medium and at a temperature below 30°C . Quite opposed to this finding is that of Bacharach (10). Using lithium nitrate instead of cupric nitrate, he obtained only the *p*-nitroacetanilide. Bacharach himself suggested that the difference is caused by the nature of the nitrate. Yet here again, when in the presence of acetic anhydride, it is probably acetanilide which results.

Thus, it is generally either an aniline salt or acetanilide which is nitrated and for this reason it is difficult to judge the orienting influence of the amino group. Only in the work of Bamberger are these complications absent. The use of nitrogen pentoxide or peroxide in an ether medium apparently gives the best results. Nitration of acetanilide also gives the ortho and para isomers and thus it would seem that the influence of the acetamino group is very close to that of the amino group. Meta substitution in excess of the other types occurs only in the presence of sulfuric or nitric acid or by conversion of aniline nitrate or phenyl nitroamine. Inasmuch as Holleman and his coworkers have shown that nitration of acetanilide in the presence of sulfuric acid with nitric or acetic acid or with acetyl nitrate all lead to some meta substitution, it seems fair to assume that meta substitution occurs normally together with ortho and para substitution. Attributing any extensive meta substitution to the presence of the amino salt group, and neglecting Bacharach's result with lithium nitrate, it then appears that the sulfuric and nitric acids reagent causes substitution in the para position, while nitrates such as acetyl nitrate, benzoyl nitrate, or cupric nitrate cause substitution mainly in the ortho position. Thus with this type of evidence it is well-nigh impossible to designate the orienting influence of the amino substituent.

The sulfonation of aniline has not received the attention it merits except in a few instances. In the first place Gattermann (73) states that sulfonation with concentrated sulfuric acid leads to a satisfactory yield of the para isomer, namely sulfanilic acid, and adds that small amounts of the ortho isomer are simultaneously formed. Though he mentions no meta substitution, Armstrong and Berry (4) report the partial conversion of aniline sulfate into *m*-anilinesulfonic acid when treated with fuming sulfuric acid. It may therefore be assumed that all three isomers are formed, at least in some cases. Of considerably greater significance, however, is the work of Bamberger and Hindermann (16) and of Bamberger and Kunz (17). They found that in the sulfonation of aniline, the sulfate was first formed, then dehydrated to give phenylsulfamic acid, which was then transformed into *o*- and *p*-anilinesulfonic acids. Furthermore, Holleman (98, p. 143) states that aniline may be converted into phenylsulfamic acid by treatment in the cold with either chlorosulfonic acid or fuming sulfuric acid. The potassium salt of this derivative treated with glacial acetic acid and a few drops of sulfuric acid and allowed to stand at 0°C. for 80 hours changes over to the extent of about 44 per cent into *o*-anilinesulfonic acid. The ortho isomer, however, when heated for 7 hours with concentrated sulfuric acid at 180–190°C., is transformed into the para acid. This change appears to be quite analogous to that of *o*-toluenesulfonic acid into its para isomer. It has already been suggested that toluene follows an

analogous reaction scheme. In any case it is of peculiar interest, since both phenol and benzoic acid are also sulfonated in a strictly similar manner.

Although sulfonation indicates the amino substituent to be a para orienting group, the evidence shows that the ortho isomer is first formed. Nevertheless the combined evidence of halogenation, nitration, and sulfonation leads to no definite conclusion, although much is thereby learned concerning the mechanism of substitution reactions.

THE HALO SUBSTITUENTS: (CHLORO-, BROMO-, AND IODO-BENZENE)

Generally, the introduction of a second substituent into the nucleus of chloro-, bromo-, or iodo-benzene is very much the same problem. Furthermore, the orienting influence of each is so nearly the same that they may profitably be considered together. For the sake of brevity, however, the evidence in regard to halogenation will not be given according to each separate investigation but rather collectively. (See, however, the supplementary references.)

The evidence as a whole shows that the presence of a catalyst such as aluminum chloride, ferric chloride or bromide, thallous chloride, aluminum, or iron, as well as heating, greatly facilitates both chlorination and bromination. Also iodination is effected through the presence of iodic, sulfuric, or nitric acids and usually heating. Although para substitution prevails, there is no evidence to prove that substitution at the other positions does not occur. Indeed, several investigators report substitution in all three positions. In each of these cases, however, a catalyst was present. Also it is apparent that no distinction can be made between the orienting influences of the three halo substituents.

Holleman and van der Linden (113) chlorinated and brominated both bromo- and chloro-benzene. Their results are presented in table 9. Although they halogenated in the presence of a catalyst in every experiment except one, this one case is sufficient to show that, even in the absence of a catalyst, substitution occurs at all three positions. In addition one can see that para substitution prevails in all cases, though a considerable amount of the ortho isomer is also formed. One should notice especially, however, the case of bromination of bromobenzene in presence of aluminum powder. The 19 to 30 per cent of the meta isomer does not substantiate the idea that ortho and para substitution are closely related and opposed to meta substitution.

But before going on to nitration, attention should be called to an investigation carried out by Copisarow (43). He showed that the action of aluminum chloride on bromobenzene caused the formation not only of dibromobenzene, of which all three isomers occurred though principally the

para isomer, but also of benzene. In a similar way Neumann (151) obtained diiodobenzene by heating iodobenzene with concentrated sulfuric acid. Apparently a halogen atom is transferred from one nucleus to another.

Concerning the nitration of these derivatives, the studies of Holleman and de Bruyn (101, 102, 106) are the most thorough and satisfactory.

TABLE 9
Halogenation of chloro- and bromo-benzene

CATALYST	ORTHO	META	PARA
a. Chlorination of PhCl at 55-75°C.			
	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
AlCl ₃	29.5 to 30	4 to 5	65.5 to 66
FeCl ₃	38.5 to 39.5	4 to 5	54 to 56
b. Chlorination of PhBr			
FeCl ₃	41.5 to 42	6 to 7	51 to 52.5
AlCl ₃	30 to 34	4.5 to 8	57 to 65
c. Bromination of PhCl			
Al powder	11 to 15	6 to 13	75 to 78
Fe powder	11 to 11.5	1.2 to 1.7	87 to 88.5
None	17.5	1.2	81.3
d. Bromination of PhBr			
Al powder	8 to 10	19 to 30	61 to 71
Fe powder	13.1 to 13.7	1.8 to 1.9	84 to 85

TABLE 10
Nitration of chlorobenzene, bromobenzene, and iodobenzene with nitric acid (1.5)

	NITRATION AT -30°C.			NITRATION AT 0°C.		
	PhCl	PhBr	PhI	PhCl	PhBr	PhI
Percent ortho isomer.	26.6	34.4	39.1	29.8	37.6	41.1
Per cent of para isomer.	73.1	65.3	60.9	69.9	62.1	58.7

Their collected results (see table 10) permit a comparison of the orienting influences of the three halo substituents and show in addition the important influence of temperature. Three points may be mentioned with regard to these results: (1) No meta substitution apparently occurs. (2) Higher temperatures favor ortho substitution. (3) The chloro substituent exerts a stronger para orienting influence than the bromo substituent just as in the case of halogenation. Thus although this reaction is normal in respect

to the temperature effect, it is abnormal with respect to the absence of meta substitution.

Although several workers studied this problem previous to Holleman, none of their work is of any significance excepting that of Coste and Parry (44). Their results are given in table 11. It is strange that the cold fuming acid gives a greater yield than the hot fuming acid. But more unusual is the fact that less *o*-nitrobromobenzene is obtained at the higher temperatures than at the lower. In all other cases of nitration higher temperatures increase the amount of ortho isomer.

As for the more recent studies, those of Schaarschmidt (175) should be mentioned. He used nitrogen peroxide in the presence of aluminum or ferric chloride to nitrate bromobenzene and obtained the ortho and para isomers in the ratio of six to ninety-four, respectively. Inasmuch as Wieland obtained the para isomer exclusively when nitrating phenol with nitrogen peroxide, these results do not seem to be caused by the catalyst

TABLE 11
Nitration of bromobenzene

NITRATING AGENT	PARA ISOMER	ORTHO ISOMER	YIELD	PARA/ORTHO RATIO
	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	
Fuming HNO ₃ at 100°C.....	65.3	34.7	66.3	1:0.53
Cold fuming HNO ₃	60.5	39.5	95.2	1:0.65
HNO ₃ (1.42) + H ₂ SO ₄	69.4	30.6	97.7	1:0.44
HNO ₃ + H ₂ SO ₄ in glacial acetic acid.....	ca. 66.0	ca. 34.0	81.4	1:0.51
HNO ₃ + H ₂ SO ₄ in glacial acetic acid.....	66.3	33.7	89.4	1:0.51

This supposition has indeed been confirmed by Schaarschmidt and his coworkers (176) in a subsequent investigation. This time they nitrated with nitrogen peroxide, but in a carbon tetrachloride solution and without a catalyst. With chlorobenzene 22 per cent of the ortho and 78 per cent of the para isomer were obtained; with bromo- and iodo-benzene, 5 per cent of the ortho and 95 per cent of the para isomers were obtained. Thus with bromobenzene the proportion of the isomers was approximately the same. Schaarschmidt himself states that the presence of the aluminum chloride, though it increased the yield to 80 to 90 per cent, produced little change in the ratio of isomers. He adds that change of temperature similarly had slight effect. In the presence of aluminum chloride, however, he has found an intermediate addition compound, 2AlCl₃·3N₂O₄·3C₆H₅Br. It may be through this compound that the aluminum chloride aids the reaction.

Quantitative yields of the para isomer from both bromo- and iodo-benzene have been obtained by Varma and Kulkarni (202), who nitrated

with a mixture of nitrosulfuric and nitric acids. By employing nitrogen pentoxide, Adkins (1) has also obtained a quantitative yield of *p*-nitrobromobenzene.

A final example of the nitration of halobenzenes is the work of Nagidson and Kalishevski (149). They state that nitration of chlorobenzene with nitric acid yields the para isomer principally, whereas nitration with sodium nitrate and sulfuric acid leads chiefly to the ortho isomer. But the formation of considerable 2,4-dinitrochlorobenzene in the latter case invalidates their conclusion.

The information concerning sulfonation is quite definite though not very extensive. In all cases the para isomer is obtained practically to exclusion of the other isomers. For instance, Otto (160) has sulfonated chlorobenzene with strong sulfuric acid. He obtained pure *p*-chlorobenzene sulfonic acid, which was proved to be the only isomer formed. More recently Ray and Day (167) have sulfonated chlorobenzene and bromobenzene at 110°C. and 100°C., respectively, using sulfuric acid (1.84) and a trace of iodine. They state that whereas other methods of sulfonation lead to a mixture of the ortho and para isomers, their method yields only the para derivative. That their results are actually caused by iodine is to be doubted. Bromobenzene has also been sulfonated by other workers, all of whom obtained only the para isomer (84, 144, 152). Chlorosulfonic acid likewise reacts with bromobenzene to yield the para isomer, as has been shown by Beckurts and Otto (21). Koerner and Paterno (131) obtained the para derivative by sulfonation of iodobenzene with concentrated sulfuric acid at water bath temperature. On the whole it appears that the same result is obtained whether chloro-, bromo-, or iodo-benzene is sulfonated. In fact, with strong acids and heating, para substitution prevails almost exclusively. No ortho substitution has been detected, yet it is possible that transformation to the para isomer has caused it to be overlooked. It is obvious that a more thorough study of this question is needed.

In view of all the experimental facts, the halobenzenes appear as the strongest of para orienting derivatives yet considered. But there is considerable evidence lacking. For instance, it is only with halogenation that substitution in all three positions is known to occur. For nitration, it is a question whether meta substitution takes place, while for sulfonation it is ortho as well as meta substitution which is doubtful. Inasmuch as all three isomers can be prepared by halogenation, it seems likely that the same should be the case for nitration and sulfonation. In general, further investigation is desirable before any more conclusions be drawn.

TABLE 12
The orienting influence of some derived substituents

SUBSTITUENT	DISUBSTITUTED BENZENES			TEMPERATURE	REFERENCE NUMBER
	Ortho	Meta	Para		
	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>degrees C.</i>	
-COCl.....	?	90.2	2.1	-10	(42)
-COOH.....	18.5	80.2	1.3	0	(100)
-CHO.....	21.4*	78.6		10	(64)
-COOMe.....	21.0 (low)	73.2	5.8 (high)	0	(100)
-COOEt.....	28.3	68.4	3.3	0	(100)
-COOC ₈ H ₁₇ (n).....	39.8*	60.2		0	(211)
-COCH ₃	45	55	—	0	(98)
-COOC ₁₆ H ₃₃ (n).....	48*	52		0	(211)
-COOCH ₂ Br.....	?	<i>m</i>	?		(119)
-CH ₂ N(CH ₃) ₂ , picrate.....	?	88	?	-5	(85)
-CN.....	<i>o</i>	80.5	(<i>p</i>)	0	(12)
-CH ₂ NH(CH ₃).....	?	69	?	-5	(85)
-CH(CN) ₂	32.1*	67.9		-10	(64)
-CCl ₃	6.8	64.5	28.7	25	(103)
-CH ₂ NMe ₂	?	58	?	0	(86)
-C(COOEt) ₃	43.4*	56.6		-10	(63)
-CH ₂ NO ₂	<i>o</i>	50	14	0	(13)
-CH ₂ NH ₂	8	49	43	0	(86)
-CH(OH)CN.....	56.4*	43.6		-9	(64)
-CH(COOEt)CN.....	62.8*	37.2		-9	(64)
-CHCl ₂	23.3	33.8	42.9	25	(103)
-CH ₂ CH ₂ NMe ₂ picrate.....	13	21	66	0	(85)
-CH ₂ CH ₂ NHMe.....	<i>o</i>	15	61	-8	(85)
-CH ₂ CH ₂ NMe ₂	20	14	66	-8	(85)
-CH ₂ CN.....	17	14	69	-13	(12)
-CH ₂ CH ₂ NH ₂	23	13	64	-5	(85)
-C≡C·COOH.....	27	7.7	65.0	-30	(12)
-CH ₂ Br.....	93*	7		17	(63)
-C≡C·COOEt.....	36	6.1	57.9	-30	(12)
-CH ₂ Cl.....	40.9	4.2	54.9	25	(103)
-CH ₃	58.0	3.9	38.1	0	(114)
-CH ₂ CH ₂ Cl.....	ca. 30	(<i>m</i>)	ca. 70	-13	(108)
-CH:CHCOOH.....	<i>o</i>	?	<i>p</i>	0	(201)
-NO ₂	4.8	93.2	1.7	0	(105)
-NH ₂ HSO ₄	2.1	46.6	51.3	-20	(107)
-NH ₂ NO ₃	5	32	62	-20	(107)
-OCH ₃	<i>o</i>	—	—		(162)
-OC ₂ H ₅	<i>o</i>	—	—		(162)
-OH.....	57.6	3.3	40.0	10	(5)

TABLE 12—*Concluded*

SUBSTITUENT	DISUBSTITUTED BENZENES			TEMPERATURE	REFERENCE NUMBER
	Ortho	Meta	Para		
	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>degrees C.</i>	
—OCOOC ₂ H ₅	(<i>o</i>)	?	<i>p</i>		(75)
—NH ₂ (in ether medium)....	<i>o</i>	—	<i>p</i>	—20	(14)
—N(CH ₃) ₂ O.....	ca. 50	?	ca. 50	0	(18)
—NH(C ₆ H ₅ CO).....	41.1	1.5	57.4	—20	(107)
—N(CH ₃ CO) ₂	40.4	1.6	58.0	—20	(107)
—N(CH ₂ C ₆ H ₅)NO.....	24	—	76	0	(170)
—NH(C ₂ H ₅ CO).....	21.1	1.2	77.7	20	(6)
—NH(CH ₃ CO).....	19.4	2.1	78.5	20	(6)
—NH(HCO).....	18.1	2.0	79.7	20	(6)
—N:CHC ₆ H ₅	5.5	0.6	93.9	20	(6)
—NO.....	?	?	<i>p</i>		(120)
—SH.....	(No data)				
—SCN.....	20	0	80	0	(32)
—SCH ₃ (sulfonation).....	10	—	90		(115)
—SCH ₃ (bromination).....	6	—	94		(115)
—SO ₂ CH ₃ (bromination)....	—	—	<i>p</i>	100	(29)
—S ₂ C ₆ H ₅ (bromination)....	—	—	<i>p</i>		(29)

* After number, signifies per cent of ortho and para isomers together.

o, *m*, and *p* signify large amounts of ortho, meta, and para isomers, respectively.

() signify smaller amounts of respective isomers.

— signifies apparent absence of respective isomer.

? signifies the formation of this isomer to be a question.

DERIVED SUBSTITUENTS

Though in concluding the discussion of the halobenzenes the principal purpose of this paper has been accomplished, it may prove of value to consider briefly some other substituents. These may be looked upon for the most part as derivatives of simpler radicals and in the presentation of the following data are therefore termed derived substituents. With a few exceptions the evidence is taken from studies on nitration. The omission of halogenation and sulfonation, where side chain substitution and molecular rearrangements are common, has been deemed advisable for the sake of comparable figures. Thus the data on the proportion of isomers formed by the mononitration of about fifty derived substituents have been collected and presented in table 12. Though strictly comparable reaction conditions are probably not attainable, figures representing such conditions were chosen where possible. Again, the effect of temperature is not very

pronounced, but it seemed advisable to indicate the approximate reaction temperature. Furthermore, the order of the substituents has been chosen primarily so as to place them in groups according to the simplest substituent to which each seems most closely related, and secondly in the order of decreasing meta substitution. When the formation of the meta isomer becomes virtually negligible, the order is that of increasing para substitution.

In several cases the relation of the type and derived substituents may not seem obvious. Thus the —COOH radical and its derivatives should belong to the toluene group. Yet the benzoic acid group is sufficiently characteristic to be placed apart. The $\text{—NH}_3\text{X}$ radicals may also seem to be misplaced, but their directive influence relates them rather to the —NO_2 than to the —NH_2 substituent. Incidentally, the covalency of the nitrogen in both the $\text{—NH}_3\text{X}$ and the —NO_2 radicals is four, as contrasted to three in the —NH_2 radical. It should also be explained that the data for aniline have been particularly chosen. The nitration was accomplished with nitrogen pentoxide in an ether medium, conditions which presumably would prevent the formation of the salt complex. Unfortunately the derivatives of thiophenol have not been investigated by nitration, and for this reason the evidence from bromination and sulfonation has been given.

Though this tabulation is presented for whatever value it may have, there are several observations which can be offered. The practically general occurrence of all three isomers, the exclusive or nearly exclusive formation of any one, and the occurrence in virtually like amounts of any two isomers to the exclusion of the third are all apparently possible results. This lack of any limitation to the proportions in which the isomers occur suggests a certain equality among them. Furthermore, it is also seen that when the percentage of either the meta or para isomer becomes overwhelming, the principal by-product is the ortho isomer. This generalization favors the view that a substituent is of either an ortho-para or ortho-meta directing type. But it must also be pointed out that if ortho substitution preponderates, the chief by-product is never the meta isomer. Under such circumstances there is an apparent relation between ortho and para substitution which is in support of the orthodox conception.

In once more considering the arrangement of table 12, it must be said that the conception according to which similar directive influences are to be expected among structurally related compounds is quite in accord with the usual point of view. Yet the —CN radical, for example, exhibits a directive influence which is scarcely similar to that of toluene. This contradiction is possibly only apparent, for there are several cases where the normally accepted directive influence of a substituent has been reversed. An excellent illustration is the nitration of benzaldehyde, as

studied by Reddelien (168). Having isolated an addition compound between benzaldehyde and nitric acid of the type $C_6H_5CHO \cdot HNO_3$, he treated it on the one hand with sulfuric acid and on the other with acetic anhydride in addition to the acid. In the former case, the chief product was *m*-nitrobenzaldehyde and in the latter case, *p*-nitrobenzaldehyde. He further indicates that whereas traces of *o*-nitrobenzaldehyde were found in both cases, on neither occasion did the para and meta derivatives occur together. Furthermore it will be recalled that benzoic acid (or more properly, the alkali benzoate) may be halogenated principally in the ortho and para positions under suitable conditions. Other examples are the introduction of the carboxyl group into the ring of benzoic acid in the ortho and para positions and similarly the mercurization of the same compound at the ortho position (6). On the other hand, the work of Shoesmith and McGechee (185) has shown how meta substitution may occur in the ring of a typical para orienting compound. They found that toluene treated with *tertiary*-butyl chloride and aluminum or ferric chloride gave *tertiary*-butyltoluenes, both meta and para, in the ratio of about seventy of the former to about thirty of the latter. And finally, the nitration of phenylboric acid is of interest in this respect. Ainley and Challenger (2) found that nitration of this compound gave 71.9 per cent of *m*-nitrophenylboric acid and 28.1 per cent of its ortho and para isomers together. But Seaman and Johnson (181), using an excess of fuming nitric acid in the presence of acetic anhydride, obtained a total yield of 65 per cent, of which 95 per cent was *o*-nitrophenylboric acid and 5 per cent its para isomer. However one may interpret such results, they inevitably suggest that a given substituent need not possess an unalterable directive influence.

It is possible that reversed directive influence is caused by a difference in the mechanism of the substitution reaction. But whether or not an explanation can be found along such lines, reaction mechanism is a factor which cannot be overlooked. Though various hypotheses have been proposed, no complete theory has been accepted. At the same time it is apparently clear that substitution reactions belong to two general classes. Thus it is usual to distinguish between direct and indirect substitution as between direct replacement of hydrogen atoms and formation of an intermediate compound with side chain. A discussion of this matter is given by Blanksma (26) and also later by Holleman (98). A very similar distinction between two types of reaction mechanism can be based on the influence of temperature. In many cases, especially those of nitration, the effect of higher temperature is invariably to increase the proportion of the ortho isomer. However in the sulfonation of several aromatic compounds, notably toluene, aniline, and phenol, the effect of higher temperature is to increase the proportion of the para isomer. The fact that molecular

rearrangements within the benzene ring are known to occur only in the second type, suggests that these are indirect reactions.

Believing therefore that such rearrangements as well as those involving the side chain are of importance, a number of interesting cases have been collected. Many of these are provided by Porter (165) incidental to his monograph on molecular rearrangements. In the first place he presents a case which throws additional light to the nitration of aniline, namely, the conversion of phenylnitroamines to nitroanilines. He says that phenylnitroamine, when warmed with sulfuric acid or dissolved in acetic acid saturated with hydrogen chloride, rearranges to form *o*- and *p*-nitroaniline. Inasmuch as phenylnitroamine is formed by nitrating aniline with nitrogen pentoxide or by warming aniline nitrate with acetic anhydride, this rearrangement would appear to play an integral part in the formation of the nitroanilines. When the para position is blocked as in 2,4-dichloro-1-nitroaminobenzene the rearrangement, following the unimolecular law, leads to the 2,4-dichloro-6-nitroaniline, corresponding to ortho substitution. But it is of some interest that 2,6-dibromo-1-nitroaminobenzene has been reported to yield a mixture of 2,6-dibromo-4-nitroaniline and 2,4-dibromo-6-nitroaniline, whereas direct nitration of 2,6-dibromoacetanilide yields only the *p*-nitro derivative (165). In commenting on these facts, Porter says that this rearrangement probably occurs regularly in the nitration of any aromatic amine. Furthermore, he says that both Armstrong and Bamberger have proposed the theory that all nucleus substitutions in aromatic amines are preceded by the formation of such addition products. In this respect it is significant, as in another example given by Porter, that the first step in the mercurization of aromatic amines has been shown to be the addition of mercuric chloride or mercuric acetate to the amino group, this being followed by a shift to the ortho or para position. That *p*-nitrodimethylaniline, which is too weak a base to form an amino-mercury salt, cannot be mercurized in the ring is offered as further evidence in favor of this mechanism.

Turning to the sulfonation of aniline, a reaction which is believed to proceed in a fashion strictly analogous to the nitration of aniline, further interesting evidence is available. Thus aniline sulfate is supposedly first formed, followed by a splitting-off of water to form phenylsulfamic acid. On heating, this yields principally the *p*- and some of the *o*-aminobenzene-sulfonic acid (73). Porter states that the temperature of the reaction determines the quantity of each of these products and that at temperatures above 180°C. the para derivative is obtained exclusively. A very similar case is that of α -naphthylamine, which on sulfonation yields first a sulfamic acid, which is subsequently converted at higher temperatures to 1-naphthyl-amino-4-sulfonic acid (73). From these cases involving aniline it seems

very probable that an addition compound is first formed by the reagent adding on to the original substituent, followed by a splitting-off of water to give a definite compound, and finally by a molecular rearrangement either to the para or the ortho position. It also seems possible that higher temperatures favor rearrangement to the para position at the expense of the ortho isomer. Whether formation of the para compound is preceded by rearrangement to the ortho position or whether it is formed directly cannot be definitely decided, although the experiment already mentioned concerning 2,6-dibromo-1-nitroaminobenzene, in which the ortho positions were both blocked by bromine atoms, might possibly mean that the ortho derivative must be formed first, for this isomer was definitely found among the products. Some support for this idea is lent by such analogous cases as the sulfonation of toluene and the sulfonation of benzoic acid, in which the ortho isomer appears to be an intermediate product.

Many other examples apparently indicating such a substitution reaction mechanism are also offered by Porter. Thus, diacetanilide rearranges on heating into the *o*- and *p*-acetylaminacetophenone, although acetanilide fails to undergo such a process. β -Phenylhydroxylamine is converted into *p*-aminophenol when heated with sulfuric acid. That the *o*-aminophenol is formed too is also implied by Porter. The transformation of acetylchloroaminobenzene into *o*- and *p*-chloroacetanilide has also received Porter's attention. He presents the following facts with regard to this rearrangement: It is unimolecular and may be brought about by exposure to light. Hydrochloric and hydrobromic acids cause a rapid and quantitative conversion to the chloroacetanilides. Although a number of workers propose that the conversion is caused by intermediate formation of hypochlorous acid or other reagents, followed by direct chlorination, further information shows that such is not necessarily the case. Thus the reaction proceeds more rapidly in non-aqueous solvents such as benzene, glacial acetic acid, or absolute alcohol than in the presence of water. The rearrangement occurs in dry benzene solution in total absence of any electrolyte, merely on exposure to light. That the conversion is actually a molecular rearrangement seems probable, especially in view of the fact that dry crystals of acetylchloroaminobenzene when exposed to light gradually go over to *o*- and *p*-chloroacetanilide and that the same change can be brought about in a few minutes by heat alone.

The formation of *p*-toluidines from alkylaminobenzenes is also discussed by Porter. This reaction has been shown to occur between two groups in the single molecule; heating seems to be necessary; and no rearrangement to the ortho position is reported to occur. Similarly, methylene derivatives such as $\text{PhNH}-\text{CH}_2-\text{NHPh}$, when warmed with hydrochloric acid or an excess of the amine hydrochloride, undergo a rearrangement which

results in the attachment of the methylene group to the para carbon atoms of the benzene nucleus. But if the para position is occupied, the migrating group goes to the ortho position. In addition to these examples, Porter also reports that triphenylmethylaniline when heated with half its weight of zinc chloride for 15 minutes at 160°C. is converted into *p*-aminotetraphenylmethane. He likewise refers to the case where, in an alcoholic or an aqueous solution of hydrogen chloride, nitrosoamines are transformed into *p*-nitrosoanilines. A final example of this class is the conversion of phenylhydrazine hydrochloride into *p*-phenylenediamine when heated to 200°C.

The numerous examples above certainly add credence to the particular mode of substitution reaction under consideration, at least with amino derivatives. But other types of benzene derivatives also provide similar evidence. The conversion of phenyl allyl ether into *o*-allylphenol, although it offers no strict analogy with any substitution reaction, is of interest (165). Porter also presents the conversion of sodium phenyl carbonate to sodium *o*-hydroxybenzoate when heated to 120–140°C. in an autoclave. Similarly potassium phenylsulfate is converted by heat into the salt of *p*-hydroxybenzenesulfonic acid. These examples are given by Porter, and he further indicates that the rearrangements go to the ortho position at lower temperatures and to the para position at higher temperatures. Another type of addition compound formation is provided by the work of Bourgeois and Abraham (29) in regard to the bromination of thio derivatives. If the transformation of benzoyl nitrate as previously described be recalled, still another type is added to the above evidence. Likewise attention should be called again to Reddelien's study concerning benzaldehyde and the author's work on the sulfonation of benzoic acid. That the sulfonation of phenol may be preceded by the formation of phenylsulfuric acid must also be remembered. With regard to the monohalogenated benzenes, there is the formation of phenyliodosochloride and its conversion to *p*-chloriodobenzene (98).

Although a majority of these examples involve amino compounds, there is actually a fair variety in which such rearrangements occur. Indeed the nature of these rearrangements indicates that introduction to the side chain followed by rearrangement to the ring is at least a possible mechanism. Though the scheme cannot be applied to all cases of aromatic substitution, it nevertheless gives a clear meaning to that type of reaction designated as indirect. Of the other type of reaction, direct substitution, no more will be said than that it is apparently characterized by direct entry of the incoming substituent to its ultimate position.

In conclusion it is hoped that, even though little attention has been given to the theoretical side, this review of just a limited portion of the experi-

mental evidence may serve to help toward a proper understanding of the problem.

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Halogenation: 25, 28, 35, 36, 47, 80, 98, 137, 161, 203, 208.
 Nitration: 66, 87, 96, 98, 100, 132, 161, 192.
 Sulfonation: 8, 50, 95, 98, 139, 156, 158, 167, 169, 171, 183.

Nitrobenzene

Halogenation: 24, 81, 126, 133, 177.
 Nitration: 1, 95, 98, 105, 163.
 Sulfonation: 56, 135, 155.

Benzenesulfonic acid

Halogenation: 61, 72, 136.
 Nitration: 135, 155.
 Sulfonation: 98, 110.

Toluene

Halogenation: 3, 7, 19, 22, 38, 39, 40, 45, 46, 48, 54, 55, 57, 60, 79, 109, 118, 122, 125, 145, 178, 179, 182, 184, 186, 187, 190, 195, 199, 200, 205.

Nitration: 23, 27, 49, 69, 77, 88, 95, 112, 114, 130, 134, 142, 146, 153, 159, 164, 172, 173, 206.

Sulfonation: 21, 62, 76, 78, 90, 104, 167.

Phenol

Halogenation: 11, 30, 33, 51, 52, 59, 83, 89, 91, 99, 111, 117, 124, 138, 141, 143, 188, 198, 204.

Nitration: 5, 9, 20, 65, 70, 74, 82, 98, 150, 162, 189, 207, 209.

Sulfonation: 98, 129, 140, 154, 157, 166, 174, 180.

Aniline

Halogenation: 34, 58, 68, 71, 94, 98, 128.

Nitration: 10, 14, 15, 31, 65, 93, 107, 116, 142, 162, 210.

Sulfonation: 4, 16, 17, 73, 98.

Halobenzenes

Halogenation: 37, 41, 43, 47, 48, 53, 98, 113, 121, 123, 127, 147, 148, 151, 193, 194, 195, 196, 197.

Nitration: 1, 44, 101, 102, 106, 149, 175, 176, 202.

Sulfonation: 21, 131, 144, 152, 160, 167.

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THE CHEMISTRY OF LIGNIN

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I. INTRODUCTION

Quite early in the development of plant chemistry, it was recognized that in the woody ("lignified") portions of plants, such as stalks, stems, cobs, hulls, leaves, trunks of trees and shrubs, there is associated with the cellulose and the other carbohydrates a substance, or a group of closely related and possibly isomeric substances, which has been designated "lignin." Schulze (264) is generally credited with having introduced this term into chemical literature, although according to Czapek (30) it had previously been employed by de Candolle (31a).

Payen (223) was the first to attempt to bring about a separation of lignified materials into their component parts. By treating wood with nitric acid and potassium hydroxide he obtained a more or less pure cellu-

lose, and pointed out that by this treatment a product richer in carbon than the residual cellulose had been removed. The material that could thus be separated from the wood by means of chemical reagents he designated "incrusting materials" ("*matieres encrustants*") and assumed that in lignified substances the cellulose was mechanically impregnated with this material. Payen's "incrustation hypothesis" was in the main supported by Schulze, who found that the incrustants, or, as he termed them, lignin, could be removed by protracted cold maceration with a mixture of nitric acid and potassium chlorate. The incrustation hypothesis has also been supported by König (175), Wislicenus (303), and more recently by Freudenberg (55). Other investigators, among them Erdmann (40), opposed Payen's views. Erdmann pointed out that whereas free cellulose dissolved readily in Schweitzer's reagent, wood substance did not, and he therefore assumed that the lignin was chemically combined with the cellulose. This view has been supported by several investigators, among them Lange (193), Hoppe-Seyler (141), Cross and Bevan (20), Grafe (86), Mehta (201), Phillips (227), and Klason (163).

There has been some speculation as to the manner in which the lignin is combined with the carbohydrate material. Some investigators (40, 193) have assumed that an ester-like union exists between an acidic group in the lignin and an hydroxyl of the carbohydrate, while others (141, 86, 201) are inclined to the view that there exists an ether-like linkage between the lignin and the cellulose or other carbohydrates. Holmberg (136) has suggested that the lignin in wood is combined with the carbohydrates in an acetal-like manner. The lignin in corn cobs seems to be dissimilarly combined with the carbohydrates, and it is assumed that part of it is combined possibly in the form of an ester, and the remainder is more firmly held, probably in the form of an ether-like combination (227).

During the past twenty years there has been a renewed interest in lignin. Besides the purely chemical investigations a great deal of work has been done in studying the microbiological transformations of this material, particularly as to its rôle in the formation of soil organic matter, peat and coal. Much work has also been done on the development of methods for the utilization of this very abundant plant material.

In this paper a review will be presented of the more important facts pertaining to the chemistry, the metabolism, and the microbiological decomposition of lignin.

II. FORMATION

There has been considerable speculation concerning the nature of the precursors of lignin. Cross and Bevan (24), König and Rump (180), and more recently Fuchs (77) have suggested that cellulose is the parent

substance from which lignin is formed. The last-named investigator pointed out in support of his hypothesis that both lignin and cellulose showed double refraction in the polarizing microscope. Other investigators, such as Klason (158) and Rassow and Zschenderlein (251), have advanced the hypothesis that lignin is formed by the plant from pentoses or pentosans. The investigators last mentioned found that plant substances high in lignin were low in pentosans and vice versa. The possibility that soluble carbohydrates, pentoses, methylpentoses, and hexoses may be used by the plant in the formation of lignin has been suggested by Schrauth (263), Schmidt (259), v. Euler (41), Odén (212), and Jonas (147). Candlin and Schryver (15) have pointed out that lignified tissues contain lignin and hemicelluloses in relatively large amounts with only traces (if any) of pectins. Non-lignified tissues, on the other hand, contain relatively large amounts of pectin, small amounts of hemicelluloses, and no lignin. Ehrlich (38) has put forward the hypothesis that pectin is the precursor of lignin. He points out that the alcohol (70 per cent)-soluble fraction of hydropectin resembles lignin in many respects; it contains methoxyl to the extent of 11.6 per cent, and its percentage of carbon and hydrogen is of the same general order of magnitude as that recorded for lignin.

It has generally been assumed that the function of lignin in the plant is to give strength and rigidity to the cell wall. However, a too high lignin content tends to make the plant tissue rather brittle. Dadswell and Hawley (31) found that brash specimens of Douglas fir had a higher lignin content than tough specimens. Phillips, Davidson, and Weihe (234) observed that lodged wheat stalks contain a greater percentage of lignin than unlogged stalks.

III. COLOR REACTIONS

Certain reagents have for many years been used by botanists and plant physiologists in testing for lignin. Nearly one hundred years ago, Runge (257) found that pine wood when treated with phenol and hydrochloric acid assumed a greenish-blue coloration, and when it was treated with aniline sulfate, a yellow color was produced. Since then, many reagents have been introduced by chemists and botanists in testing for lignin. Organic and inorganic reagents have been employed. Among the former, the "phloroglucinol reagent," or "Wiesner's reagent," which gives a reddish-violet coloration with lignified material, has been widely used in testing for lignin. Other organic compounds, such as primary and secondary amines, have also been used in examining for lignin. The colors produced when lignified tissues are treated with phenols and with amines are given in tables 1 and 2, respectively.

In the case of the phenols the reaction is carried out by first moistening

the plant material with dilute hydrochloric acid and then applying to it an aqueous solution of the phenol (if the phenol is insoluble in water, an alcoholic solution is employed). Grandmougin (87) recommends that a 0.1 molar solution of phenol in 60 per cent ethanol be used. With amino compounds the reaction is carried out by adding a 1 per cent solution of the base in dilute hydrochloric or sulfuric acid. However, with dimethyl-*p*-phenylenediamine the aqueous solution of the neutral sulfate is used.

TABLE 1
Color reactions given by phenols and lignified materials

PHENOL	COLORATION	INVESTIGATOR
Phenol.	Greenish-blue	Runge (257, 87)
<i>o</i> -Cresol.	Greenish-blue	Grandmougin (87)
<i>m</i> -Cresol.	Blue	Grandmougin (87)
<i>p</i> -Cresol.	Green	Grandmougin (87)
Thymol.	Green	Czapek (29, 143)
Catechol.	Blue	Wiesner (299)
Resorcinol.	Blue	Wiesner (299)
Hydroquinone.	Olive	Grandmougin (87)
Phloroglucinol.	Violet-red	Wiesner (299)
Pyrogallol.	Green	Wiesner (299)
1,2,3,5-Tetrahydroxybenzene.	Green	Fuchs (74)
Orcinol.	Dark red	Lippmann (196)
<i>o</i> -Nitrophenol.	Yellowish olive	Grandmougin (87)
<i>m</i> -Nitrophenol.	Yellowish olive	Grandmougin (87)
<i>p</i> -Nitrophenol.	Yellowish olive	Grandmougin (87)
<i>o</i> -Aminophenol.	Yellow	Grandmougin (87)
<i>m</i> -Aminophenol.	Yellow	Grandmougin (87)
<i>p</i> -Aminophenol.	Brownish-yellow	Grandmougin (87)
Lepidin.	Red	Ihl (143)
α -Naphthol.	Greenish-blue	Grandmougin (87)
β -Naphthol.	Rose	Grandmougin (87)
1,2-Dihydroxynaphthalene.	Light green	Fuchs (74)
1,4-Dihydroxynaphthalene.	Flesh color	Fuchs (74)
1,5-Dihydroxynaphthalene.	Dirty green	Fuchs (74)

The question whether the color reactions given by aromatic substances with lignified tissues can be attributed to some characteristic group of the lignin complex or to some minor constituent associated with the lignin has been a controversial subject for many years. Singer (275) considered that the coloration was possibly due to vanillin and coniferin. This was, however, challenged by Seliwanow (270). Nickel (209) made the rather interesting observation that wood behaves like an aldehyde towards Schiff's reagent (fuchsin and sulfur dioxide) and that wood treated with

sodium bisulfite solution was no longer colored by the aniline sulfate reagent. Subsequently Czapek (28) isolated a substance which he called "hadromal" by digesting wood with stannous chloride solution and extracting the residue with benzene. From ligroin "hadromal" separated out as a brown crystalline substance melting at 70–80°C. "Hadromal" had phenolic and aldehydic properties and readily gave the various lignin color reactions.

TABLE 2
Color reactions given by amines and lignified materials

AMINE	COLORATION	INVESTIGATOR
Aniline.....	Yellow	Runge (257)
<i>o</i> -Toluidine.....	Yellow	Grandmougin (87)
<i>m</i> -Toluidine.....	Yellow	Grandmougin (87)
<i>p</i> -Toluidine.....	Yellow	Grandmougin (87)
<i>o</i> -Nitroaniline.....	Yellow	Grandmougin (87)
<i>m</i> -Nitroaniline.....	Orange	Grandmougin (87)
<i>p</i> -Nitroaniline.....	Orange	Bergé (7)
1-Methyl-2-amino-6-nitrobenzene.....	Yellow	Grandmougin (87)
<i>o</i> -Phenylenediamine.....	Orange-brown	Grandmougin (87)
<i>m</i> -Phenylenediamine.....	Yellow	Molisch (205)
<i>p</i> -Phenylenediamine.....	Orange-brown	Grandmougin (87)
Toluylenediamine (1-methyl-2,5-diaminobenzene).....	Orange	Hegler (111)
Dimethyl- <i>p</i> -phenylenediamine.....	Red	Wurster (304)
<i>p</i> -Aminodiphenylamine.....	Bordeaux-brown	Grandmougin (87)
Benzidine.....	Orange	Schneider (260)
α -Naphthylamine.....	Orange-yellow	Nickel (210)
β -Naphthylamine.....	Orange-yellow	Nickel (210)
Diphenylamine.....	Golden orange	Ellram (39)
Pyrrole.....	Red	Ihl (143)
Indole.....	Cherry-red	Niggl (211)
Skatole.....	Cherry-red	Mattirolo (199)
Thalline.....	Orange	Hegler (110)
Carbazole.....	Cherry-red	Mattirolo (199)

Grafe (86) considered the "hadromal" of Czapek a mixture of vanillin, methylfurfural, and catechol. However, since Grafe employed a different method for preparing "hadromal" (extraction of wood with 10 per cent hydrochloric acid or heating with water under pressure at 180°C. for 1 hour) than that described by Czapek, his results cannot be accepted as evidence against the homogeneity of "hadromal."

Crocker (19) and recently Hoffmeister (134) have confirmed Czapek's results. The last-named investigator, by employing essentially the Czapek method, succeeded in isolating "hadromal," and judging from the analysis

and the chemical behavior of this substance considered it identical with coniferyl aldehyde. This conclusion has since been questioned by Pauly and Feuerstein (220). This leaves the question of the homogeneity and identity of "hadromal" unanswered, and accordingly a reinvestigation of this subject would be most desirable.

In summing up, it may be stated that the evidence thus far adduced indicates that most of the so-called lignin color reactions given by lignified tissues with aromatic compounds are due to an aldehydic substance possibly in the nature of "hadromal" (coniferyl aldehyde?), which is closely associated with the lignin complex.

Color reactions with inorganic reagents

Casparis (16) found that a solution of cobalt thiocyanate colored lignified tissue blue.

When lignified materials are chlorinated, as in the Cross and Bevan method for the determination of cellulose, and then treated with a dilute sodium sulfite solution, a pink to a purple-red coloration is produced (8). This is a very sensitive test and is apparently given by some characteristic group of the lignin complex.

Cross and Bevan (22) found that lignified tissues react with a ferric ferri cyanide solution to form Prussian blue, which is attached to the fiber. Crocker (19) has shown that this test can be given by many reducing substances and is therefore too general in character and cannot be considered a "lignin reaction."

A reaction which has also been used in testing for lignin is the so-called Mäule (200) reaction. Lignified material when left in a 1 per cent potassium permanganate solution for 5 minutes, washed, treated with dilute hydrochloric acid, washed, and then immersed in an ammonia solution, acquires a deep red color. According to Browne (11a) the reaction appears to be due to a deposition of manganese dioxide on the wood. This reacts with the hydrochloric acid to produce chlorine, which forms the compound that turns red with alkalis. Chlorine water can be used in place of the potassium permanganate and hydrochloric acid, and any alkali or organic base can replace ammonia, but usually not with advantage (19).

de Lamarlière (32) found that gymnosperms did not give a red coloration by the Mäule reaction. This was confirmed by Schorger (261). Crocker (19) subjected to the Mäule reaction eighteen species of deciduous woods, including the interesting balsa wood, eighteen species of coniferous woods, and ginkgo wood. All the woods of deciduous angiosperms gave distinct red colors. All those of coniferous gymnosperm, and of the deciduous gymnosperm, *Ginkgo biloba*, gave only indefinite yellow or pale brown colors. Crocker's work was later extended by Sharma (272).

Combes (18) has described the following lignin reaction: The material is treated with a hypochlorite solution for 15 minutes, washed, heated on the water bath for 15 minutes with 1 g. of zinc oxide suspended in 30 cc. of water, washed, treated with hydrogen sulfide for 10 to 15 minutes, and finally treated with a few drops of sulfuric acid. A red coloration is produced which later changes to orange red, and finally to brown.

A lignin color reaction has been described by Podbrenznik (246), which depends on the action of hydrochloric acid and potassium chlorate. When warmed with this reagent, pine wood and lignin gave an orange color, which turned yellow on addition of ammonia.

Morquer (206) observed that lignin was stained bright red and cellulose violet by treating sections of plant tissue as follows: (1) Six minutes in an aqueous solution of sodium hypochlorite, and (2) 10 minutes in a 2 per cent solution of phloroglucinol in alcohol. The material is transferred to a watch glass and two drops of an iodine solution (0.5 g. of iodine, 1 g. of potassium iodide, 20 cc. of water) and eleven drops of freshly prepared hydriodic acid solution are added and allowed to react for 1 minute. The excess reagent is removed and one drop of glycerol that has been acidulated with hydriodic acid is added.

IV. QUANTITATIVE ESTIMATION

The various methods that have been described in the literature for the quantitative estimation of lignin may be classified as direct and indirect. In the direct methods, the lignin is separated from the other plant constituents and weighed as such. In the indirect methods either some characteristic group of lignin, such as the methoxyl group, is determined and by multiplication with a suitable factor the percentage of lignin is computed or advantage is taken either of the fact that lignin produces a coloration with certain reagents or of some other characteristic chemical property of lignin.

Indirect methods

1. *Method of Schulze.* The oldest indirect method for determination of lignin is that due to Schulze (264). Schulze oxidized lignified plant material with nitric acid and potassium chlorate and assumed that the loss in weight represented the lignin. This method is only of historical interest as the results obtained by it are much too high, for not only is the lignin completely oxidized by the drastic oxidizing reagent employed but the hemicelluloses and perhaps some of the cellulose are also destroyed.

2. *Method of Benedikt and Bamberger* (6). Benedikt and Bamberger determined the percentage of methoxyl in a large number of woods and showed that there was a close relationship between the percentage of

methoxyl and the lignin content as determined by the method of Schulze (264). However, the method of Schulze is now known to give erroneous results owing to the fact that other constituents in the wood are determined along with the lignin. The method of Benedikt and Bamberger is based on the assumption that in lignified plant materials lignin is the only substance containing the methoxyl group and that the methoxyl content in lignin from various sources is the same. Neither of these assumptions is entirely true. This method for determining lignin is chiefly of historical interest and is hardly ever used now.

3. *Method of Cross, Bevan, and Briggs* (25). This method is based on a reaction between lignin and phloroglucinol and is carried out as follows; Two grams of finely ground and dry (100°C.) wood is treated with 40 cc. of phloroglucinol solution (2.5 g. of phloroglucinol in 500 cc. of hydrochloric acid, d. 1.06). The flask is stoppered, and the reaction mixture shaken from time to time and allowed to stand overnight. The reaction mixture is filtered and 10 cc. of the filtrate taken for titration. To this solution, 20 cc. of hydrochloric acid (d. 1.06) is added and the resulting solution warmed to 70°C. A furfural or formaldehyde solution (2 g. of furfural in 500 cc. of hydrochloric acid, d. 1.06, or 2 cc. of 40 per cent formaldehyde solution in 500 cc. of hydrochloric acid, d. 1.06) is then added from a burette in portions of 1 cc. After each addition of the aldehyde solution, the reaction mixture is allowed to stand for 2 minutes while the temperature is maintained at 70°C. A drop of the reaction mixture is placed on cheap newspaper, and if unreacted phloroglucinol is present, a red spot is obtained. Toward the end of the reaction, the aldehyde solution is added in portions of 0.25 cc., and the testing is done by placing a drop of the solution on the paper and holding it over the Bunsen flame (20 cm. away) for 1 minute. When the reaction is complete, no red spot on the paper is obtained. Ten cc. of the original phloroglucinol solution is titrated in a similar manner, and the amount absorbed by the lignocellulose obtained by difference. The results are expressed as per cent of the dry weight of lignocellulose taken for analysis.

A comparison was made by Venkastewaran (287) between the results obtained by this method and those given by the 72 per cent sulfuric acid method and the fuming hydrochloric acid method. The phloroglucinol absorption method was found to give much higher results than the other two methods. This the author believes is due to the absorption of phloroglucinol by the furfural-yielding groups.

The method of Cross, Bevan, and Briggs has been somewhat modified by Votoček and Potměšil (288), who determine the excess phloroglucinol gravimetrically by precipitation with furfural. Neumann (208) determines the excess phloroglucinol by titration with a solution of diazotized *p*-nitroaniline.

4. *Method of Seidel* (269). This method is based on the fact that when nitric acid is added to lignin, oxides of nitrogen are given off. For carrying out the determination a special apparatus is required, and the quantity of oxides of nitrogen produced is determined by titration with permanganate. By the use of an empirical factor, the percentage of lignin in the sample can be calculated.

5. *Method of Waentig and Gierisch* (290). This method is based on the fact that lignin takes up a considerable quantity of chlorine, and by determining the amount of chlorine absorbed it is possible to estimate the percentage of lignin. The weighed sample is placed in a special apparatus and a stream of dry chlorine gas passed through until no further increase in weight of the sample is noted. A stream of dry air is then passed through the apparatus to remove the excess chlorine. The per cent increase in weight corresponds to the "chlorine number." The "chlorine number" when divided by 1.4 gives the percentage of lignin in the sample. (The factor 1.4 is employed because lignin isolated from wood by the fuming hydrochloric acid method has a chlorine number of 140.)

Semmler and Pringsheim (271) applied this method to the determination of lignin in straws and fodders and found that the results agreed reasonably well with those obtained by direct methods. However, in the case of straw which had been treated by Beckmann's method, the analytical procedure of Waentig and Gierisch gave results which were decidedly high.

6. *Method of Mehta* (201). Taking advantage of the fact that a solution of phosphotungstic and phosphomolybdic acids in phosphoric acid is a very sensitive reagent for detecting minute amounts of aromatic substances containing hydroxyl groups, Mehta has developed a micro method for the estimation of lignin. The reagent is prepared in accordance with the directions of Folin and Denis (53). A standard solution of lignin in dilute sodium hydroxide is prepared so that 1 cc. equals 1 mg. of lignin. Known volumes (1.0 to 0.1 cc.) of the standard lignin solution are accurately measured out into Nessler cylinders and to each is added 2.5 cc. of the phosphotungstic-phosphomolybdic reagent and after 5 minutes 12.5 cc. of a saturated solution of sodium carbonate. The volume is made up to 100 cc., and the colors are matched with that obtained under similar conditions from an unknown amount of lignin.

Direct methods

The direct methods for the quantitative estimation of lignin may be divided into two classes: (1) Those that depend upon dissolving cellulose and other carbohydrates and leaving the lignin as an insoluble residue; and (2) those that dissolve out the lignin and thus separate it from the cellulose and other carbohydrate material. As examples of the first class may be

mentioned the 72 per cent sulfuric acid and the fuming hydrochloric acid methods, whereas the method of Mehta (201) is an example of the second class.

The methods of class 1 are most commonly employed for the quantitative estimation of lignin. It must be pointed out, however, that these methods are not altogether accurate. In fact, any method based on weighing a "residue" cannot be considered satisfactory. Among the objectionable features of these methods may be mentioned (1) the possibility of incomplete hydrolysis of the carbohydrates, (2) the formation of reversion products from the carbohydrates, and (3) contamination of the lignin residue with nitrogenous complexes. In the determination of lignin in such materials as corn cobs, corn stalks, hay, bran, hulls, and similar agricultural materials, the "lignin" residue obtained always contains a substantial amount of nitrogen.

1. *Sulfuric acid method.* In 1883 Flechsig (52) showed that 72 per cent sulfuric acid will hydrolyze cellulose in the cold. This fact has been applied by Klason (154) and by Ost and Wilkening (214) to the quantitative estimation of lignin. König and Rump (181) subjected the plant material to a preliminary extraction with an alcohol-benzene solution and then hydrolyzed it with 72 per cent sulfuric acid until a sample of the product when treated with iodine and sulfuric acid showed no blue coloration when observed through the microscope. Schwalbe and Becker (265) subjected flax and hemp chaff to a preliminary hydrolysis with hydrochloric acid (d. 1.19) and extraction with hot water before treatment with 72 per cent sulfuric acid. The sulfuric acid method in slightly modified form has been used by Becker (3), Dore (34), Mahood and Cable (197), Paloheimo (215), Venkateswaran (287), and Müller and Hermann (207). According to von Euler (42), several corrections must be applied when the sulfuric acid method is used, in order to obtain "rational" lignin values. To correct for the acetic acid split off from the lignin, the per cent of crude lignin must be increased by 2 per cent. To this must be added the percentage of alcoholic extractives (found after the wood has been given a preliminary extraction with benzene), which von Euler believes properly belongs to the lignin fraction. From the final results 5.7 per cent is deducted for the sulfuric acid that cannot be removed from the lignin by washing. The errors, however, balance, so that the lignin content of Norway spruce as determined by Becker's method is approximately correct. Thus, Norway spruce when analyzed by Becker's method gave 30.5 per cent of lignin. The alcohol extractives amounted to 3.5 per cent. The "rational" lignin value is then $30.5 + 2 + 3.5 - 5.7 = 30.3$ per cent.

Klason (166) has modified his original procedure and recommends that 64 or 66 per cent sulfuric acid be used in place of the 72 per cent acid. To

1 g. of ground wood which has been extracted with ether and dried at 100°C., 50 cc. of 66 per cent sulfuric acid is added, and the mixture is stirred with a glass rod until the gelatinization is complete. The following day the mixture is again stirred and allowed to stand for another day. It is then diluted with water, and the lignin is filtered in an alundum crucible and washed with water until the filtrate is free from sulfuric acid. Fifty cc. of 0.5 per cent hydrochloric acid is then added, and the mixture digested on the steam bath for 12 hours. The hydrochloric acid is then removed by filtration and the lignin washed with water until free from sulfuric acid. The lignin is first dried at 75°C. and for one-half hour at 100°C., then weighed, ashed, and reweighed. The weight of lignin is obtained by difference.

The U. S. Forest Products Laboratory method is described by Bray (11) as follows: Two grams of air-dry wood, sawdust, or shredded pulp is weighed into a tared alundum crucible (porosity R.A. 98) contained in a glass-stoppered weighing bottle. The crucible and its contents are dried to constant weight at 105°C. and weighed. The material is then extracted with ether in a Soxhlet for three to four hours. (In the case of pulps the extraction with ether is not necessary.) The dry material is transferred from the crucible to a weighing bottle and treated with 40 cc. of 72 per cent (± 0.1) by weight of sulfuric acid, the strength of which is determined by titration against standard alkali. The hydrolysis is allowed to proceed for 16 hours at room temperature with frequent stirring and thorough mixing of the acid with the sample at the beginning of the operation. The resulting product is transferred to a 2-liter Erlenmeyer flask and diluted to 1570 cc. with distilled water (which makes the concentration of the sulfuric acid 3 per cent). It is then covered with a watch glass and boiled for 2 hours, distilled water being added from time to time to keep the volume constant. The lignin is filtered off on the tared alundum crucible used in the beginning of the determination, washed thoroughly with hot distilled water (500 cc.), dried at 105°C., and weighed.

Ritter, Seborg, and Mitchell (252) proposed the following modification of the above method: (1) The residue after the extraction with alcohol-benzene should be extracted with hot water for 3 hours; (2) the concentrated acid-wood mixture should be kept in a bath at 20°C., and 2 hours should be allowed for solution of the carbohydrates in the 72 per cent sulfuric acid; (3) the diluted mixture is hydrolyzed for 4 hours. Their analytical procedure is as follows:

"Approximately 2 grams of air-dried sawdust (60 to 80, or 80 to 100 mesh) are weighed in a tared alundum crucible. The crucible and its contents are dried to constant weight at 105°C., cooled, and weighed. The material is then extracted for 4 hours in a Soxhlet apparatus with a minimum boiling solution of alcohol-benzene.

The solvent is removed by suction; the residue is washed with alcohol by suction to remove the benzene, and then extracted with 400 cc. of hot water in a water bath for 3 hours, filtered, washed with hot water, then with alcohol, and finally dried. Washing the residue with alcohol aids in the removal of the sawdust from the crucible after drying.) The dried residue is transferred to a glass-stoppered weighing bottle, and is well mixed with 25 cc. of 72 per cent sulfuric acid at 20°C., and maintained at that temperature for 2 hours. The resulting mixture is transferred to an Erlenmeyer flask, diluted with water to make a 3 per cent acid solution, and then boiled for 4 hours under a reflux condenser. The hydrolyzed residue is filtered on a tared alundum crucible, washed free of acid by means of hot water, dried, and weighed. The lignin content is calculated on the basis of the oven-dry sample.

"In case a correction for ash is desired, transfer the lignin residue to a tared platinum dish and ash the usual way.

"In determination of lignin in chemical pulps, 40 cc. of 72 per cent sulfuric acid should be used for dissolving the carbohydrates present in a 2-gram sample. The water extraction may be omitted with all chemical pulps and the alcohol benzene may be omitted with alkaline-cooked pulps.

Ross and Hill (255) add formaldehyde solution to the 72 per cent sulfuric acid-wood mixture. The time required for the hydrolysis of the carbohydrates is thereby considerably reduced. Wise and Fairbrother (302) found that in the case of hardwoods, the U. S. Forest Products Laboratory method invariably gave higher lignin than the Ross and Hill method, but if the material is previously extracted with hot water and alcohol-benzene solution, the results are in approximate agreement. In the case of coniferous woods, however, the Ross and Hill method gives the higher values.

Waksman and Stevens (295) hydrolyze the residue remaining after extracting the plant material successively with ether, cold and hot water, alcohol and dilute acid, with 80 per cent sulfuric acid. From the weight of the crude lignin the weight of ash and crude protein is deducted.

Peterson, Walde, and Hixon (224a) have called attention to the fact that in determining lignin by the 72 per cent sulfuric acid method, the temperature of the acid should be below 15°C., as otherwise too high values for lignin are obtained. They recommend that the temperature of the sulfuric acid should be between 4° and 15°C.

Cohen and Dadswell (17) found that the usual 72 per cent sulfuric acid method failed to give satisfactory results when applied to wood of the Eucalyptus family. By first digesting the wood with 0.125 *N* sodium hydroxide at 98–100°C. for 80 minutes, the interfering substances could be removed. The lignin could then be determined in the usual way. It seems quite likely, however, that the preliminary digestion with alkali removes part of the lignin along with other substances (107).

2. Fuming hydrochloric acid method. In 1913 Willstätter and Zechmeister (301) recorded the observation that fuming hydrochloric acid (d. 1.212 to 1.223 at 15°C.) will completely hydrolyze cellulose in the cold. This

principle has been applied by Krull (184) to the determination of lignin. Five grams of wood moistened with 15 cc. of water is placed in a Claisen flask, cooled with ice, and saturated with hydrogen chloride gas, generated by dropping concentrated sulfuric acid into concentrated hydrochloric acid. After standing twenty to twenty-four hours most of the hydrochloric acid is removed by heating the reaction mixture to 70°C. at 14 to 19 mm. pressure. It is then diluted with water, boiled for 8 hours under a reflux condenser, and the lignin filtered off.

König and Becker (179) use 6 cc. of water to 1 g. of wood to secure greater fluidity and then saturate this with hydrogen chloride gas. Dore (34) uses ordinary concentrated hydrochloric acid instead of water and then passes a stream of hydrogen chloride gas through the concentrated hydrochloric acid containing the sample in suspension.

Schwalbe and Becker (266) add 60 cc. of fuming hydrochloric acid (d. 1.21) to 1 g. of wood which has been previously extracted with alcohol-benzene solution and allow the mixture to stand in a cool place for 24 hours. The product is then filtered off, washed with water, dried, weighed, and ashed, and the crucible is reweighed.

Semmler and Pringsheim (271) applied the fuming hydrochloric acid method to the determination of lignin in straw and feedstuffs. The sample was mixed with the acid and allowed to remain in the ice chest for two days. It was then diluted with water, and filtered, and the precipitate again hydrolyzed with the fuming hydrochloric acid. *

Heuser and Skiöldebrand (124) treated the purified wood with fuming hydrochloric acid (d. 1.212) and allowed it to stand for several days in a cool place. The product was then filtered, and washed with water, and the precipitate again treated with fuming hydrochloric acid. The hydrolysis with the strong acid was continued until a sample of the acid filtrate no longer gave a test for reducing sugars with Fehling's solution.

A modification of the hydrochloric acid method has been introduced by Wenzl (298), who used a mixture of phosphorus pentoxide and concentrated hydrochloric acid (30 g. of phosphorus pentoxide to 100 cc. of concentrated hydrochloric acid) to remove the polysaccharides.

Schwalbe (268) used a mixture of hydrochloric acid (d. 1.07) and 72 per cent sulfuric acid for hydrolysis of the cellulose and the other carbohydrates associated with it.

Paloheimo (217) has made a critical study of the fuming hydrochloric acid method as applied to the determination of lignin in feedstuffs. The method is subject to two possible errors: (1) incomplete hydrolysis of proteins; (2) formation of "reversion products" or humus-like material when the hydrolyzed product is diluted with water before filtration. To eliminate the second error, Paloheimo has devised a special apparatus in

which the strong acid is in contact with the plant material for only a short time and the acid removed by filtration. The disturbing influence of the substances yielding "reversion products" may also be eliminated by giving the plant material a preliminary treatment for half an hour with 1.25 per cent potassium hydroxide solution. The results obtained by the method of Paloheimo are very much lower than those obtained by the other methods. In determining the lignin content of hay, straw, stalks, and similar agricultural materials, it is undoubtedly good practice to determine the percentage of nitrogen in the crude lignin and to make the proper deductions. The pre-treatment of the plant material with potassium hydroxide solution is, however, of doubtful value, as some lignin is unquestionably removed by this treatment, thus giving low values for lignin.

A detailed description of the fuming hydrochloric acid method for determination of lignin has been given by Phillips (233). The crude lignin obtained is analyzed for its percentage of nitrogen and ash. The weight of lignin in the sample is computed as follows: Weight of lignin equals weight of crude lignin minus weight of ash, minus weight of nitrogen, times 6.25. In this procedure the presumption is, of course, made that the nitrogenous residue is in the nature of a protein. While this is perhaps not entirely justified, in view of the present knowledge of the chemistry of lignin, it is possibly the best procedure to follow.

Billington, Simmonds, and Baird (9) made a study of four methods for determination of lignin, namely, the Forest Products Laboratory Method (197, 11), the modified Forest Products Laboratory method (252), the Ross and Potter method (255), and the method of Willstätter and Zechmeister (301). They conclude that the Willstätter and Zechmeister method possesses the greatest inherent accuracy. The modified Forest Products Laboratory method is slightly less accurate than the method of Willstätter and Zechmeister, but has the advantage over the latter in facility of operation and speed. The Ross and Potter method gave in every case a lignin fraction having the lowest percentage of methoxyl, whereas the lignin isolated by the method of Willstätter and Zechmeister contained the highest percentage of methoxyl.

3. *Method of König and Rump* (182). In this method the hydrolysis of the cellulose and the other carbohydrates associated with it is brought about by heating the sample for 5 hours with 1 per cent hydrochloric acid under a pressure of 5 to 6 atmospheres. The lignin residue obtained is tested for cellulose with the iodine-sulfuric acid reagent, and if a positive reaction is obtained the heating with hydrochloric acid is repeated.

4. *Alkali method—method of Mehta* (201). This method is based on the fact that the lignin fraction in a lignified plant material can be removed by heating the latter with alkali under pressure. Five grams of the sample

and 100 cc. of 4 per cent sodium hydroxide solution are heated for 1 hour under a pressure of 10 atmospheres. The alkaline solution is then filtered and made up to a definite volume, and an aliquot is acidified with hydrochloric acid. The lignin precipitate is filtered off, washed with water, and redissolved in boiling 95 per cent ethanol. The alcoholic solution is filtered, and the filtrate evaporated to dryness, dried, and weighed. The lignin values obtained by this method are considerably lower than those obtained either by the fuming hydrochloric acid or the 72 per cent sulfuric acid methods, owing probably to the partial degradation of the lignin by the sodium hydroxide solution heated to a comparatively high temperature.

V. ISOLATION

Whatever method for the isolation of lignin is used, it is important that the finely ground plant material be first freed from various "extractives," such as fatty substances, resins, and volatile oils. This is generally accomplished by extracting the lignified material with ether and ethanol or acetone and ethanol, but preferably with a 1:2 alcohol-benzene solution. This may be followed by an extraction with cold and hot water. Some investigators, such as Friederich and Diwald (70), give the plant material a preliminary treatment with 5 per cent sodium hydroxide solution in order to remove gummy substances. Freudenberg, Zocher, and Dürr (65) remove the gums from the wood with sodium hydroxide solution and then reflux the residual material with 1 per cent sulfuric acid. When the material is degummed with sodium hydroxide solution, there is, however, the danger of losing some of the lignin because of its solubility in this reagent.

It may be stated at the very outset that there is as yet no method known by which lignin can be isolated unchanged. Whatever method is employed, a lignin preparation is obtained which is no longer identical with the natural lignin—the claims of some investigators to the contrary notwithstanding. In the methods described below for the isolation of lignin, preparations are obtained that are more or less related to the lignin as it occurs naturally in the plant. This should not be taken as implying that all methods are of equal value from the standpoint of one who is interested in studying the chemistry of lignin. Some methods are more drastic than others and yield therefore considerably degraded lignin preparations.

The various methods described in the literature for the isolation of lignin may be conveniently divided into two classes: (1) Those that depend on the removal, by hydrolysis, of the cellulose and other components, leaving the lignin as an insoluble residue, and (2) those that depend on the removal of lignin from the cellulose and the other substances with which it is associated.

Methods of class 1

1. *Sulfuric acid method.* For the isolation of lignin by this method, 72 per cent sulfuric acid is generally employed, although lower concentrations of acid (64, 66, and 70 per cent) have also been used. Although it has long been known that strong sulfuric acid will dissolve cellulose at ordinary temperatures, this acid was first made use of by Klason for the isolation of lignin from wood.

2. *Method of Klason* (154). For every gram of wood, 10 cc. of 70 to 72 per cent sulfuric acid is added. The reaction mixture is stirred and allowed to stand until a sample of the product no longer gives a test for cellulose. The product is then poured in water, filtered, and washed with cold and with hot water.

The method described above has since been modified by Klason (167). The ground and sifted wood is first extracted with ether and then dried at 100°C. For every gram of wood, 50 cc. of 66 per cent sulfuric acid is employed, and the mixture stirred until gelatinization is complete. It is then allowed to stand for 48 hours with frequent stirring. The reaction product is diluted with water, filtered, and washed with water. To remove the combined sulfuric acid, the reaction product is heated on the steam bath for 12 hours with 0.5 per cent hydrochloric acid. The product is washed with water until free of acid and dried.

Paloheimo (218) employed 70 per cent sulfuric acid for the isolation of lignin.

A modification of the sulfuric acid method has recently been proposed by Sherrard and Harris (273). They hydrolyze the lignified material at 10°C. with 70 per cent sulfuric acid. Dry sawdust previously extracted with 1:2 alcohol-benzene solution and with water is added (in the proportion of 10 cc. of acid to 1 g. of wood) to 70 per cent sulfuric acid previously cooled to 10°C. The reaction mixture is shaken until gelatinization occurs (about three minutes) and again placed in the cooling bath. After about one hour, when the mixture begins to thin, it is again shaken for a few minutes to insure contact of the acid with all the sawdust. It is then allowed to stand for 15 hours in the cooling bath at 10°C. It is diluted with water (37 to 38 volumes), and well stirred, and the mixture is boiled under a reflux condenser for 4 hours. The product is filtered and washed with hot water.

3. *Fuming hydrochloric acid method.* This method was first proposed by Willstätter and Zechmeister (301). These investigators found that hydrochloric acid of 42 to 43 per cent strength readily dissolved cellulose, leaving the lignin as an insoluble residue. Lignin prepared by this method, or its modifications, is frequently referred to in the literature as "Will-

stätter lignin." The fuming hydrochloric acid (d. 1.212 to 1.223 at 15°C.) required for this method may be prepared as follows (187, 233): To 500 g. of sodium chloride contained in a liter Pyrex distilling flask provided with a ground glass stopper, a cold solution of 250 cc. of water in 450 cc. of concentrated sulfuric acid is added. The side tube of the distilling flask is connected to a glass tube which passes through a sulfuric acid wash bottle. The outlet tube of the sulfuric acid wash bottle is connected to another glass tube which is immersed in a flask containing 3 liters of concentrated hydrochloric acid. The flask containing the hydrochloric acid is surrounded with crushed ice. The distilling flask is heated with a small flame, and the hydrogen chloride gas is passed into the acid solution until it attains the specific gravity of 1.212 to 1.223 at 15°C. The fuming hydrochloric acid thus prepared is stored in a refrigerating room.

According to Schwalbe and Ekenstam (267), in the isolation of lignin by the Willstätter method from both sound and rotted wood, the residual lignin is liable to contain cellulose, owing to the rapid swelling action of the highly concentrated acid and the consequent prevention of diffusion of the acid to the interior of the wood. This difficulty may be overcome by treating the wood with relatively dilute acid (25 per cent) and gradually increasing the concentration of the acid to 42 per cent. Under these conditions, the lignin is more rapidly and completely freed from cellulose, and the product obtained is more easily filtered.

a. Method of Willstätter and Kalb (300). The following is a description of the procedure followed by Willstätter and Kalb for the isolation of lignin by the fuming hydrochloric acid method: Pine sawdust is successively extracted with water, 80 per cent acetone, and pure acetone, and finally dried. Two hundred grams of this pretreated sawdust is added, with stirring, to 4 liters of fuming hydrochloric acid, and the mixture is allowed to remain at room temperature for 4 hours. To this, 1300 g. of ice is added in small portions and allowed to stand for 18 hours. Finally, 1300 cc. of water is added, and the mixture is then filtered. The lignin precipitate is washed with dilute hydrochloric acid and then with water. It is finally boiled with water, and the acid in the aqueous solution carefully neutralized with soda. A light brown lignin preparation is obtained. Yield, 26 to 28 per cent of the weight of the starting material.

A modification of this method is given by Kürschner (187). The method, however, is rather troublesome to carry out and difficulty is experienced in obtaining a lignin preparation entirely free from cellulose.

b. Method of Kalb and Lieser (148). This method is a modification of that of Willstätter and Kalb. One hundred grams of dry wood flour is added to 2 liters of hydrochloric acid (d. 1.222 at 0°C.) and cooled to 1°C. to 5°C. The reaction mixture is well stirred and allowed to stand for 2

hours. To this, 650 cc. of water or ice is added, and the mixture allowed to remain at room temperature for 18 hours more. It is then diluted with another 650 cc. of water, and the lignin is filtered off and washed successively with 2 liters of 1:1 hydrochloric acid, water, very dilute soda solution, and hot water. Yield, 25 per cent of the weight of the starting material.

Kalb and Lieser (148) have described another modification of the fuming hydrochloric acid method. The extracted wood is first hydrolyzed with fuming hydrochloric acid for 2.5 hours at 0°C. The product is poured into ice, filtered, and washed with water and with dilute ammonia. It is then treated with a cuprammonium solution (prepared by adding copper carbonate to 25 per cent ammonia solution), and the mixture is allowed to stand overnight and then shaken for 4 hours in a shaking machine. The product is filtered off and washed with dilute hydrochloric acid, water, and dilute ammonia solution.

Bremer (12) failed to obtain a carbohydrate-free lignin preparation by treating pine wood flour with 2 liters of 42 per cent hydrochloric acid at 0°C. for 24 hours. It was only after five successive treatments with the 42 per cent acid that it was possible to obtain a preparation which was free from carbohydrates.

A modification of the hydrochloric acid method has been proposed by Kucher (185). He employs a mixture of hydrochloric acid (d. 1.18) and sulfuric acid (d. 1.84) for the hydrolysis of the cellulose.

4. *Method of Urban* (286). Urban avoids the use of fuming hydrochloric acid and strong sulfuric acid for the hydrolysis of the polysaccharides. Twenty grams of extracted wood is treated with a mixture consisting of 1350 cc. of hydrochloric acid (d. 1.18) and 450 cc. of phosphoric acid (d. 1.7) and allowed to remain for fifty to sixty hours at 20°C. The product is filtered, washed with a fresh portion of the hydrochloric-phosphoric acid mixture, then successively with concentrated hydrochloric acid, dilute hydrochloric acid, and hot water, and finally extracted with acetone and again washed with water.

Freudenberg and Harder (58) have used the method described above for the isolation of lignin. The wood was, however, first degummed with 5 per cent sodium hydroxide solution according to the method of Friedrich and Diwald (68). This preliminary treatment of the wood with alkali unquestionably results in the partial removal of the lignin along with the gums.

5. *Method of Freudenberg and coworkers* (61). In this method the lignin is isolated by alternately hydrolyzing wood with boiling 1 per cent sulfuric acid and cuprammonium solution. However, it must be pointed out that the latter reagent not only dissolves cellulose but also to some extent lignin (285), so that the yield by this method is somewhat lower. Ground and

extracted (alcohol-benzene solution) pine wood is digested in the cold with 5 per cent sodium hydroxide solution for 24 hours. The alkali is then poured off and the residue similarly treated with a fresh quantity of 5 per cent sodium hydroxide solution. The product is filtered, washed with water, dilute acetic acid, and again with water. To remove pentosans and hemicelluloses, it is boiled with 1 per cent sulfuric acid. The product is shaken in a shaking machine for 12 hours with Schweitzer's reagent (prepared by adding an excess of copper turnings to 25 per cent ammonia, cooling to 0°C., and passing through the solution a mixture of air and ammonia gas for 8 hours). The reaction mixture is centrifuged and the precipitate washed with Schweitzer's solution, concentrated ammonia, water, dilute hydrochloric acid, and again with water. The operation of boiling with 1 per cent sulfuric acid and treating with Schweitzer's solution is repeated three times.

Using the method described above, Freudenberg obtained a lignin preparation which was light brown in color and contained 16 per cent methoxyl. When this was treated for 5 hours with a solution consisting of 3 volumes of hydrochloric acid (d. 1.19) and 1 volume of syrupy phosphoric acid, a product was obtained which was darker in color, but the methoxyl content of the preparation had increased to 17 per cent.

Methods of class 2

1. *Sulfite method.* This method for the removal of lignin is of considerable industrial importance, and has been the basis of the preparation of wood pulp for many years. The delignification is brought about by heating wood with acid sulfites under pressure. By this method lignin is obtained not in the free state but in the form of water-soluble sulfonic acids. A description of these acids will be given elsewhere.

2. *Alkali method.* This method of isolation of lignin has been used by a number of investigators. Both aqueous and alcoholic sodium hydroxide solutions have been employed. The ease with which lignin can be obtained by this method depends somewhat on the character of the lignified plant material. In case of cereal straws and corn cobs, for example, lignin fractions can be obtained by treatment with alcoholic or aqueous sodium hydroxide solutions in the cold, whereas in the case of wood a more drastic treatment is required.

Methods of Beckmann, Liesche, and Lehmann (4). (1) Aqueous sodium hydroxide.—Rye straw cut in small pieces (1 part) is treated with 8 parts of 1.5 per cent aqueous sodium hydroxide solution and allowed to remain at room temperature for two days. The product is filtered and the straw pressed. To the alkaline filtrate sufficient hydrochloric acid is added so that there is 2 to 2.5 per cent free acid per liter, and the solution

is boiled for 5 to 10 minutes. The product is filtered and washed with water. Yield, 9.5 per cent of the weight of dry straw.

(2) Alcoholic sodium hydroxide.—In this method the pentosans and hexosans are removed with alcohol. The extraction of the lignin is carried out as in (1) except that an alcoholic sodium hydroxide solution (prepared by dissolving 20 g. of sodium hydroxide in 400 cc. of water and adding 600 cc. of 96 per cent ethanol) is used. The alkaline-alcoholic extract is neutralized with hydrochloric acid, and most of the alcohol is distilled off under reduced pressure. The residual solution is made acid with hydrochloric acid, and the lignin filtered off and washed with water. Beckmann, Liesche, and Lehmann, using this method for the isolation of lignin from winter rye straw, obtained a yield of 5.2 per cent, which could be increased to 7 per cent by subjecting the straw to three successive extractions with the alcoholic sodium hydroxide solution.

Employing a method similar to that above described, Phillips (226) isolated a lignin fraction from corn cobs in 3.49 per cent yield. The product was a light yellow amorphous powder.

Powell and Whittaker (241) isolated lignin from flax shoves by heating it with 10 per cent sodium hydroxide solution under pressure. The yield was 20 to 22 per cent of the weight of the flax shoves taken. These investigators have also applied this method to the isolation of lignin from wood. In the case of wood, however, a somewhat higher temperature was employed, 140–160°C. (243).

Mehta (201) isolated lignin in 15.6 to 17.1 per cent yields by heating wood with 4 per cent sodium hydroxide solution under 8 atmospheres pressure for 1 to 1.5 hours. A similar method has been employed by Dorée and Barton-Wright (35). The lignin fraction which they isolated was designated "metalignin." The product was found to be soluble in organic solvents.

Phillips (227) isolated four lignin fractions from corn cobs by "fractional extraction." The corn cobs, previously extracted with an alcohol-benzene solution, were subjected to extraction with a 2 per cent alcoholic sodium hydroxide solution until a test sample upon removal of the alcohol and subsequent acidulation no longer gave any precipitate of lignin (fraction A). The residual material was successively extracted with a 2 per cent aqueous sodium hydroxide solution at 100°C. until the extract was free from lignin (fraction B). The residue from this treatment was similarly extracted with a 2 per cent aqueous sodium hydroxide solution at 135°C. (fraction C) and finally with a 4 per cent sodium hydroxide solution at 180°C. The total yield (calculated on the corn cobs treated) amounted to 9.0 per cent and was distributed among the four fractions as follows: (A) 4.4 per cent; (B) 3.7 per cent; (C) 0.84 per cent; and (D) 0.14 per cent. The cellulose residue obtained from the final treatment was entirely free from lignin.

By a similar procedure two lignin fractions were isolated from oat hulls (229).

3. *Separation of lignin by alcoholysis.* The isolation of lignin by heating wood with various hydroxylic compounds in the presence of catalysts has come into use during the past few years. Grüss (89) in 1920 recorded the observation that lignin could be isolated from wood by heating the latter with alcohol and hydrochloric acid. This reaction has been applied by Friedrich and Diwald (70), Friedrich and Brüda (67), Hägglund and Rosenqvist (104), Hägglund and Urban (106), Fuchs (80), Campbell (14), Hibbert and Rowley (130), Hibbert and Marion (127), Hibbert and Phillips (129), Rassow and Gabriel (247), Rassow and Lüde (248), Fuchs and Daur (82), and Kleinert and Tayenthal (170). In place of ethanol other hydroxy compounds have been used, such as butyl and amyl alcohols (106), ethylene glycol (130, 127, 247, 248), the monomethyl ether of ethylene glycol (80, 127), and glycerol α -monochlorohydrin (129). In all cases a product is obtained containing the alkyl or aryl group, as the case may be, in combination with the lignin. The mechanism of the reaction between the hydroxy compound and the lignin is not clear. It has been suggested by Hägglund (106) that a product in the nature of an acetal is formed. However, the evidence available as to the acetal character of the lignin-alcohol complex seems to be inconclusive.

a. Method of Friedrich and Diwald (70). Finely ground pine wood which had been extracted with alcohol-benzene solution and degummed with 5 per cent sodium hydroxide solution is treated with an equal weight of hydrochloric acid (1 volume of hydrochloric acid, d. 1.17, and 1 volume of water), thoroughly mixed and allowed to stand for 48 hours. To the reaction mixture ten times its weight of 96 per cent ethanol is added, and then it is refluxed for eight to ten hours. The reaction product is filtered, and the dark brown filtrate concentrated to one-third its original volume. The concentrated filtrate is poured into ten times its volume of water to which a little hydrochloric acid has been added. The precipitated product is purified by redissolving in alcohol and reprecipitating. The freshly prepared material is soluble in alcohol, acetone, acetic acid, ethyl acetate, and in sodium hydroxide solution. It gives a strong reaction with the phloroglucinol-hydrochloric acid reagent. This lignin preparation has been designated by Friedrich and Diwald as "primary" lignin. When heated with hydriodic acid, as in the Zeisel determination of alkoxyl groups, it yields ethyl iodide and methyl iodide, the ethyl iodide arising from the ethyl alcohol used in the isolation of this lignin fraction (104).

b. Amyl-lignin (method of Hägglund and Urban) (106). Forty grams of ground pine wood which has been extracted with acetone is treated with 800 cc. of isoamyl alcohol and 50 cc. of 37 per cent hydrochloric acid and

refluxed for 45 minutes. The reaction product is filtered, and the filtrate freed from hydrochloric acid and sugars by extraction with water. It is then concentrated under reduced pressure. The residue is dissolved in warm dilute sodium hydroxide solution, and filtered, and the filtrate acidified with hydrochloric acid. The precipitate is filtered, washed with water, and redissolved in glacial acetic acid and reprecipitated with water.

c. "Isobutyl-lignin" has similarly been prepared by Hägglund and Urban (106).

d. "Methylglycol-lignin" (Fuchs (80)). Four grams of wood flour, 60 cc. of the monomethyl ether of ethylene glycol, and 1 cc. of concentrated hydrochloric acid are heated together under a reflux condenser for 24 hours. The reaction product is filtered, and the "methylglycol-lignin" precipitated by the addition of water.

Details for the isolation of lignin with ethylene glycol (so-called glycol-lignin) are given by Hibbert and Rowley (130), Hibbert and Marion (127), and by Rassow and Gabriel (247).

4. *Extraction of lignin with phenols.* The fact that lignin can be extracted from wood with phenols was first noted by Bühler (13). As in the case of the extraction of lignin with alcoholic compounds, the phenols also combine chemically with the lignin, yielding the so-called phenol lignin. According to Kalb and Schoeller (149), "phenol-lignin" may be prepared by heating pine sawdust with phenol and hydrochloric acid for 1 hour at 90°C. The reaction product is filtered, and the filtrate steam-distilled to remove the excess phenol, whereupon the lignin preparation remains in the distilling flask.

Among others who have described the preparation of "phenol-lignin" may be mentioned Legeler (194), Hillmer (132), and Wedekind, Engel, Storch, and Tauber (296).

5. *Other methods.* Karrer and Widmer (151) found that wood, straw, and similar materials, when treated for several hours with acetyl bromide, dissolve completely. This solution, when poured on ice, yields a precipitate from which a bromo derivative of lignin may be separated.

Friedrich (66) obtained a lignin preparation by treating wood meal with a mixture of 1 volume of glacial acetic acid and 0.03 volume of concentrated hydrochloric acid at 100°C. The reaction product was filtered, and the lignin preparation obtained by the addition of water to the filtrate. The product was hydrolyzed with alkali hydroxide to remove combined acetic acid.

A rather interesting method for the separation of a lignin fraction from wood has recently been reported by Küster and Daur (192). They treated extracted beechwood flour with diazotized sulfanilic acid in the presence of sodium hydroxide solution. The dissolved lignin was precipitated with

β -naphthylamine hydrochloride or with *p*-bromoaniline hydrochloride. Küster and Daur believe that this method of isolating lignin causes the least decomposition in the lignin molecule. An objectionable feature of the method, however, is the fact that part of the cellulose is also dissolved by the diazobenzenesulfonic acid treatment.

TABLE 3
Elementary composition of various lignin preparations

SOURCE	METHOD OF ISOLA- TION	CAR- BON	HYDRO- GEN	INVESTIGATOR
		<i>per cent</i>	<i>per cent</i>	
Flax	A	63.9	5.8	Powell and Whittaker (241)
Larch	A	63.8	5.2	Powell and Whittaker (243)
Pine	A	63.4	5.6	Powell and Whittaker (243)
Spruce	A	64.0	5.5	Powell and Whittaker (243)
Ash	A	63.2	5.6	Powell and Whittaker (243)
Birch	A	63.2	5.5	Powell and Whittaker (243)
Poplar	A	63.3	5.8	Powell and Whittaker (243)
Corn cobs	A	62.5	5.0	Phillips (227)
Oat hulls	A	64.4	5.2	Phillips (229)
Rye straw	B	63.0	5.6	Beckmann, Liesche, and Lehmann (4)
Corn cobs	B	61.1	5.8	Phillips (226)
Spruce	C	62.4	6.4	Heuser, Schmitt, and Gunkel (122)
Spruce	C	64.0	5.3	Hägglund (94)
Spruce	D	63.9	5.3	Klason (165)
Spruce	E	63.9	6.0	Urban (286)
Wood	E	64.7	5.5	Freudenberg and Harder (58)
Spruce	F	63.6	5.7	Freudenberg, Zocher, and Dürr (65)

A, aqueous sodium hydroxide method.

B, alcoholic sodium hydroxide method.

C, fuming hydrochloric acid method.

D, sulfuric acid method.

E, method of Urban.

F, Freudenberg method.

VI. ELEMENTARY COMPOSITION

The elementary composition of the lignin complex varies somewhat with the source and with the method employed for its isolation. A few of the many results on the elementary analysis of lignin found in the literature are given in table 3, from which it will be observed that, considering the fact that the various investigators were never absolutely certain as to the purity of their preparation, the agreement is fairly good.

VII. CONSTITUENT GROUPS

The presence of the methoxyl group ($-\text{OCH}_3$) has been definitely established in the lignin preparations isolated from various sources and by

different methods. The methoxyl groups of lignin are not readily split out, from which it is inferred that they are attached in the form of an ether linkage rather than an ester linkage as in the case of the pectins. The absence of other alkoxyl groups, such as ethoxyl ($-\text{OC}_2\text{H}_5$), has been definitely established in the case of spruce (105) and oat hull lignin (230).

According to Freudenberg (56), the methoxyl groups present in lignin are attached to aromatic nuclei. He studied the rate of removal of the methoxyl groups of lignin with hydriodic acid and found that this corresponded approximately to that of vanillin. In the case of an aliphatic substance like 3-methylglucose, 96 per cent of the total methoxyl was split out in 20

TABLE 4
Percentage of methoxyl in various lignin preparations

SOURCE	METHOD OF ISOLATION	METH-OXYL	INVESTIGATOR
		<i>per cent</i>	
Spruce.....	A	14.47	Klason (156)
Fir.....	A	13.95	König and Rump (176)
Fir.....	A	16.40	König (174)
Sugar maple.....	A	21.00	Sherrard and Harris (273)
Spruce.....	B	14.39	Hägglund (90)
Spruce.....	B	13.10	Fischer and Schrader (47)
Spruce.....	B	11.60	Kürschner (186)
Flax.....	C	14.90	Powell and Whittaker (241)
Winter rye straw.....	D	14.85	Beckmann, Liesche, and Lehmann (4)
Corn cobs.....	D	12.10	Phillips (226)
Corn cobs.....	C	14.30	Phillips (228)
Oat hulls.....	C	15.80	Phillips (229)
Oat hulls.....	D	15.61	Phillips (229)

A, sulfuric acid method.

C, aqueous sodium hydroxide method.

B, fuming hydrochloric acid method.

D, alcoholic sodium hydroxide method.

minutes, whereas in vanillin and lignin a much longer reaction period was required to accomplish this.

The methoxyl content of lignin varies somewhat with the source and the method employed for the isolation of the lignin. Phillips (227) found that the methoxyl content of lignin from corn cobs varied with the temperature employed for the isolation of the lignin. In table 4 are given a few of the many methoxyl determinations recorded in the literature.

The presence of hydroxyl groups in lignin is indicated by the fact that it can be acetylated and alkylated. Alcoholic as well as phenolic hydroxyl groups seem to be present. Powell and Whittaker (241) acetylated lignin isolated from flax shives by the aqueous sodium hydroxide method, and

found that the acetylated product was insoluble in cold sodium hydroxide solution, thus indicating that the acidic character of their lignin preparations was due to phenolic hydroxyl groups. Freudenberg (65) contends that in the lignin isolated by his method no free phenolic hydroxyl groups are present.

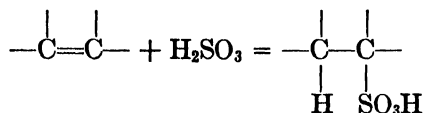
The fact that wood and similar lignified materials when distilled with dilute mineral acids afford formic and acetic acids has caused several investigators to assume that lignin contains acetyl and formyl groups (26). However, the presence of either acetyl or formyl groups in any of the lignin preparations has not been established, and from the evidence thus far presented no definite conclusion can be drawn as to their presence or absence in natural lignin.

The evidence as to the presence of carbonyl groups in lignin preparations is rather inconclusive. Powell and Whittaker (241) found that their lignin preparation reduced Fehling's solution and concluded from this that an aldehydic group was present. However, it must be remembered that substances other than aldehydes can reduce Fehling's solution, so that the claim of Powell and Whittaker must be accepted with considerable reserve. Friedrich and Diwald (69) obtained condensation products of an indefinite character of "primary lignin" with phenylhydrazine and semicarbazide. According to Hägglund (102), no free carbonyl groups are present in Willstätter lignin, although treatment of this material with acid in the presence of phenols and aromatic amines discloses their presence.

Freudenberg (59) found that lignin isolated from wood by Urban's method when distilled with 12 per cent hydrochloric acid yields formaldehyde (0.7 per cent of weight of lignin). This investigator has accordingly advanced the hypothesis that the formaldehyde arises from a methylene dioxide group ($-\text{O}-\text{CH}_2-\text{O}-$) present in the lignin molecule, as compounds containing this group are known to yield formaldehyde when they are distilled with hydrochloric acid. Phillips and Goss (236) isolated lignin from corn cobs, oat hulls, and spruce wood by the fuming hydrochloric acid method, by the alcoholic and aqueous sodium hydroxide methods, and by Freudenberg's modification of Urban's method. These lignin preparations were distilled with 12 per cent hydrochloric acid. Formaldehyde was found in an appreciable quantity only in the distillate from the lignin isolated from oat hulls by the Freudenberg and Harder modification of Urban's method and in the distillate from the lignin from spruce wood prepared by the same method. The percentage of formaldehyde obtained by these investigators from the lignin of spruce wood was in substantial agreement with that recorded by Freudenberg and Harder (59). However, if the theory of Freudenberg were to be accepted that the formaldehyde arises from a methylene dioxide group present in the lignin molecule, the

conclusion would have to be drawn that this group is present only in lignin isolated from certain plant materials. Furthermore, it is rather difficult to conceive how such a mild treatment as that employed in the isolation of lignin by the alcoholic sodium hydroxide method could bring about the removal of such a comparatively stable group as the methylene dioxide group. It seems questionable, therefore, whether the formaldehyde that is obtained in the hydrolysis of certain lignin preparations can be considered as a fission product of a methylene dioxide group. Recently, Freudenberg (64) presented evidence of a rather indirect character as to the presence of the methylene dioxide group in lignin. Altogether, however, the presence of this group in lignin must be regarded with some uncertainty.

The presence of the ethylenic bond in lignin has not been definitely established. To account for the formation of rather stable ligninsulfonic acids by the interaction of lignified material with sulfurous acid and bisulfites, Klason (159) assumed that an ethylenic bond is present in lignin and that the formation of the stable sulfonic acid takes place in this fashion:



Data on the halogenation of lignin are rather inconclusive. According to Freudenberg (56), when lignin prepared by his method is brominated, substitution takes place but no addition. On the other hand, Hibbert (131) working with "glycol-lignin" found that addition of bromine as well as substitution took place.

VIII. ACYLATION

Pringsheim and Magnus (245) acetylated Willstätter lignin with acetic anhydride and pyridine. The acetyl content of the product varied considerably with the source of the lignin, as is seen from table 5.

A systematic study of the acetylation of Willstätter lignin from pine wood was made by Heuser (114). He employed five acetylation methods. Products containing the highest percentages of acetyl were obtained when acetic anhydride and pyridine or acetyl chloride were used as the acetylating agents.

By heating alkali lignin from flax shives with acetic anhydride in the presence of a few drops of concentrated sulfuric acid, Powell and Whittaker (241) obtained a product which was insoluble in sodium hydroxide solution and which contained 20.4 per cent of acetyl.

Phillips (226) acetylated the lignin fraction (isolated from corn cobs by

the alcoholic sodium hydroxide method) with acetic anhydride in the presence of sulfuric acid and obtained a product which contained 17.3 per cent acetyl.

The two lignin fractions isolated from oat hulls by the alcoholic and the aqueous sodium hydroxide methods gave acetyl derivatives which assayed 16.8 and 16.2 per cent acetyl, respectively (229).

Fuchs and Horn (85) acetylated Willstätter lignin with acetic anhydride containing sulfuric acid and obtained an acetylated lignin with 19.2 per cent acetyl. Elementary analysis, coupled with the determination of methoxyl and acetyl, indicated the presence of four methoxyl and four acetyl groups in a compound represented by the formula $C_{50}H_{52}O_{20}$. Lignin as it occurs naturally in wood can be acetylated so that the product appears to contain three acetyl groups in excess of those present in acetylated Willstätter lignin. It appears, therefore, that isolated lignin must be so altered by the hydrochloric acid treatment that its activity toward acetylation is diminished.

TABLE 5
Acetyl content of acetylated Willstätter lignin

SOURCE OF LIGNIN	ACETIC ACID
	<i>per cent</i>
Pine wood	19.85
White beech	37.85
Straw	27.20

The acetylation of wood with the subsequent separation of the acetylated lignin fraction has been reported by Suida and Titsch (278, 279) and by Friese (73).

Beckmann, Liesche, and Lehmann (4) prepared a benzoyl derivative of alkali lignin from winter rye straw by treating the lignin with benzoyl chloride and pyridine. Results of the analysis of the benzoylated product for carbon and hydrogen indicated the presence of four benzoyl groups. The same investigators also prepared *p*-bromobenzoyl and *p*-nitrobenzoyl derivatives.

A benzoyl derivative of "primary lignin" has been prepared by Friedrich and Diwald (70).

A *p*-toluenesulfonyl derivative of lignin isolated from pine wood by the method of Urban (286) has been prepared by Freudenberg and Hess (62). Five grams of lignin was suspended in 250 cc. of 2 *N* sodium hydroxide solution, stirred mechanically, and 50 g. of *p*-toluenesulfonyl chloride in 200 cc. of benzene was added at room temperature in the course of ten hours.

The reaction product was filtered off, and the above operation repeated. Yield, 8.5 g. The product contained 7.0 per cent of sulfur.

Benzoyl derivatives of ligninsulfonic acid have been prepared by Klason (155) and by Dorée and Hall (36).

IX. ALKYLATION

Lignin can be readily alkylated by the usual alkylating reagents. Heuser and coworkers (122) methylated lignin, isolated from wood by the fuming hydrochloric acid method, by suspending 5 g. of lignin in 100 cc. of 10 per cent sodium hydroxide solution and adding gradually 30 g. of dimethyl sulfate and maintaining the temperature at 60°C. The original methoxyl content was thereby increased from 14.65 per cent to 20.73 per cent. By repeated methylation, a product was finally obtained containing 26.29 per cent of methoxyl. Lignin which had previously been heated with sodium hydroxide in an autoclave at 170°C. yielded a product which contained 24.69 per cent of methoxyl. Another sample of lignin containing 14.15 per cent of methoxyl gave on repeated methylation a product with 26.05 per cent of methoxyl (120).

Holmberg (137) methylated with dimethyl sulfate and alkali two fractions of alkali lignin which he designated as α and γ alkali lignin. The methoxyl percentage of the α -fraction was increased from 15.45 to 23.41 and that of the γ -fraction was increased from 14.6 to 23.16 per cent.

The lignin fraction isolated by Powell and Whittaker (241) from flax shoves was readily methylated with dimethyl sulfate and 3 per cent sodium hydroxide solution. The methylated product (25.6 per cent methoxyl), unlike the original lignin, was no longer soluble in alkali and therefore, presumably, no longer contained free phenolic hydroxyl groups (71).

Urban (286) methylated lignin with dimethyl sulfate and 45 per cent potassium hydroxide at 80–100°C. After fifteen successive methylations a product was obtained containing 28.23 per cent of methoxyl. However, if the temperature during the methylation was controlled so that it did not exceed 25°C., a product was obtained after two successive methylations which contained 32.4 per cent of methoxyl.

Lignin prepared by Urban's method was treated with an ether solution of diazomethane, and after two days the percentage of methoxyl increased from 15.5 to 19.8 per cent (63). Fuchs and Horn (84), employing a different technic, obtained similar results. They treated pine wood with diazomethane and obtained a product which contained about 16 per cent of methoxyl and from which a lignin with 19.7 per cent of methoxyl could be isolated. Since the original lignin isolated by the treatment with hydrochloric acid contained 15.4 per cent of methoxyl, it follows that one hydroxyl group susceptible to methylation with diazomethane is present in a

molecule having a molecular weight of about 800. The methylated lignin exhibited double refraction.

Klason (162) methylated calcium ligninsulfonate. Heuser and Samuelson (120) methylated ligninsulfonic acid by adding 10 g. of the acid to 200 g. of 10 per cent sodium hydroxide solution and treating with 65 g. of dimethyl sulfate. The methoxyl content of the product amounted to 20.67 per cent and this could be increased to 25.43 per cent by five successive methylations. The product after the sixth methylation had the same methoxyl percentage as that from the fifth, thus indicating that 25.43 is the maximum percentage of methoxyl that can be introduced in ligninsulfonic acid, at least under the conditions employed by the above investigators. The methylated product was light yellow in color, but when exposed to the air it became darker in color. It was insoluble in water, ether, petroleum ether, and mineral acids, and very slightly soluble in ethanol.

X. HALOGENATION

The chlorination of the lignin complex was first studied by Cross and Bevan (21). By the chlorination of jute they obtained a substance, represented by the formula $C_{10}H_{18}Cl_4O_9$ (26.8 per cent chlorine), which they designated "lignone chloride." This substance dissolved in alkaline solutions and in glacial acetic acid and alcohol. "Lignone chloride" was believed to be closely "allied to mairougallol and leucogallol."

Heuser and Sieber (123) in similar manner studied the action of chlorine on spruce wood. After two hours the wood absorbed 31 per cent of its weight of chlorine. The chlorinated product was extracted with absolute alcohol and a product was obtained which contained 47 per cent of carbon, 4.6 per cent of hydrogen, and 22.7 per cent of chlorine. The percentage of chlorine was therefore considerably less than that recorded by Cross and Bevan for their "lignone chloride." Heuser and Sieber were unable to obtain the chloropyrogallol derivatives from chlorinated lignin as claimed by Cross and Bevan.

Hägglund (92) chlorinated Willstätter lignin at 0°C. and obtained a product which contained 46 per cent of chlorine. The sublimation of this product afforded no chloroquinone nor any trichloropyrogallol.

According to Jonas (145), if Willstätter lignin is chlorinated under carefully controlled temperature conditions, the same chlorolignin derivatives are always obtained.

A rather drastic method of halogenation has been employed by Tropsh (284). He refluxed Willstätter lignin with antimony pentachloride containing a small amount of iodine and obtained perchloroethane and hexachlorobenzene.

"Primary lignin" in acetic acid solution was brominated by Friedrich and Diwald (70). A product was obtained which was not homogeneous, and methoxyl determinations made on this material indicated that considerable degradation of the "primary lignin" had taken place.

Powell and Whittaker (241) passed a stream of dry chlorine through a suspension of alkali lignin in carbon tetrachloride. They obtained a brick-red solid, soluble in alkalies, which contained 35.1 per cent of chlorine. Phillips (226), working in a similar manner with alkali lignin from corn cobs, isolated a chlorinated lignin product which contained 32.1 per cent of chlorine.

Alkali lignin from straw was treated by Paschke (219) with sulfuryl chloride at room temperature and a pale brown amorphous product, $C_{37}H_{42}S_3Cl_3O_{12}$, was obtained. When the halogenation was performed at 100°C. in a sealed tube, a product was obtained which contained 38.2 per cent of chlorine and was free from sulfur.

Fuchs and Horn (83) treated acetylated wood with a solution of bromine in carbon tetrachloride in the presence of iodine as a catalyst. Hydrolysis of the bromoacetylated wood with acid afforded a lignin preparation having 11 per cent of bromine.

Fuchs (79) treated a suspension of 2 g. of dry Willstätter lignin in 25 cc. of carbon tetrachloride with a 4 per cent solution of bromine in the same solvent and with a small crystal of iodine as a catalyst, and refluxed the mixture for 20 minutes. A product was obtained which contained 11.4 per cent of bromine. Part of the bromine could be removed by boiling with a 5 per cent sodium acetate solution.

Chlorolignins produced in the chlorination process from woody fibers were found to have a mean content of chlorine of 30 per cent, if extracted by an organic solvent. Lime precipitated chlorolignin from soda solution, hence the disadvantages attached to the use of lime and bleaching powder in processes for cellulose production (289).

Freudenberg, Belz, and Niemann (56) treated lignin (isolated from spruce wood by the Freudenberg method) with a solution of bromine in hydrobromic acid and found that under these conditions substitution took place but no addition. Polymerized coniferyl alcohol behaved similarly, thus indicating that neither substance contained a double bond. However, Hibbert and Sankey (131), working with glycol-lignin, found that on the assumption of a molecular weight of 400 for lignin, the bromine absorbed indicated 1 to 1.5 ethylenic bonds in this substance. Whether this difference in results can be attributed to the fact that different lignin preparations were used by Freudenberg and by Hibbert is not known. It is evident, however, that a critical study of the halogenation of lignin will be necessary before any conclusion can be drawn regarding the presence or absence of ethylenic bonds in this substance.

Friedrich and Pelikan (72) found that when spruce wood lignin is brominated a loss of methoxyl takes place to the extent of 30 per cent of the original methoxyl content. Since all the methoxyl groups could not be removed by the bromination, these investigators assumed that the methoxyl groups in lignin are not similarly combined. The maximum amount of bromine taken up by lignin was 38.7 per cent, of which 28 per cent was firmly bound. When brominated lignin was alkylated with diazomethane, 28 per cent of the bromine was split out.

XI. NITRATION

Lignin is nitrated very readily. Tropsch and Schellenberg (282) obtained an amorphous nitro substance by treating lignin with 5 *N* nitric acid. The readiness with which lignin is nitrated, these investigators believe, indicates that it has a phenolic constitution.

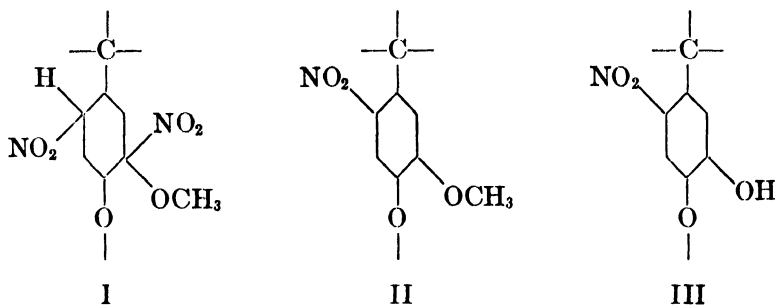
Nitrolignin was prepared (50) by treating 150 g. of Willstätter lignin, with cooling, with 1 liter of 5 *N* nitric acid. The reaction mixture was then warmed until the product became uniformly orange colored. The product was purified by dissolving in alcohol, cooling the solution with ice and salt, and precipitating the nitrolignin by passing in dry hydrogen chloride gas. From 20 g. of the crude material only 11.5 g. of purified nitrolignin was obtained. It had the composition $C_{42}H_{37}N_3O_{24}$. The percentage of nitrate nitrogen in this preparation, as determined by the method of Silberrad, Phillips, and Merriman (274), was found to be 44. Acetylation yielded a product containing 15.5 per cent of acetyl. Reduction with tin and hydrochloric acid afforded a brown polymerized product which contained 3.27 per cent of nitrogen as against 4.34 per cent in the original nitrolignin.

Powell and Whittaker (242) obtained a nitrolignin by adding portionwise 15 g. of lignin (isolated from flax shoves by the alkali method) to a solution consisting of equal parts of sulfuric and nitric acids cooled to -5°C . The reaction mixture was poured into water, and the nitro product separated out as an amorphous red precipitate which was soluble in alcohol and acetone. It was readily acetylated, and a product containing 18.9 per cent of acetyl was obtained.

Lignin from various sources when nitrated with 5 *N* nitric acid was found to yield compounds of a similar character. According to Fuchs (78) they are isonitrosoketohydroxylcarboxylic acids of high molecular weight and have a cyclic structure.

Lignin was found to react very rapidly with gaseous nitrogen dioxide (258). After a short period the initial absorption was succeeded by evolution of nitric oxide resulting from a secondary oxidation. With methylated lignin only the initial rapid absorption was observed. During the reaction the lignin became partly demethylated, with the production of methanol.

These observations were explained on the assumption that substitution had occurred. Under favorable conditions the ratio of nitrogen introduced to the original aromatic methoxyl approached 1:1. Double linkings were not involved to an important extent, since nitrolignin and nitromethyl-lignin could be brominated and bromomethyl-lignin could be nitrated. Loss of methoxyl from lignin or methyl-lignin was considered due to addition of nitrogen dioxide yielding compound I, which in part lost nitrous acid to give compound II and in part eliminated methyl nitrite, giving a quinol derivative passing into the nitrophenol III (57).



Glycol-lignin (obtained by digesting wood which had been extracted with an alcohol-benzene solution with ethylene glycol at 110°C. in the presence of a catalyst, such as iodine or hydrochloric acid), was readily nitrated by adding it to a mixture consisting of 4 parts of acetic anhydride and 1 part of fuming nitric acid (d. 1.49) maintained at temperatures below 0°C. Acetylation occurred simultaneously. The nitrated lignin contained 8.65 per cent of total nitrogen, 3.18 per cent of ester nitrogen (NO_3), 2.57 per cent of combined nitro (NO_2) and nitroso (NO) nitrogen. The character of the remaining nitrogen (2.89 per cent) was not determined. The nitrated lignin could be methylated and could also be reduced with sodium amalgam in alkaline solution. The resulting reduction product could be diazotized, and the latter when coupled with β -naphtholdisulfonic acid afforded a product which dyed silk and wool a brownish color when mordanted with tannic acid (128).

Kürschner (190) nitrated lignin with an alcoholic solution of nitric acid (1 volume of nitric acid and 4 volumes of alcohol). The nitrated product was crystalline. This, however, requires confirmation.

Methylated lignin (27.2 per cent methoxyl), prepared from lignin isolated from corn cobs by the alkali method, when treated with 5 *N* nitric acid afforded an orange-colored amorphous product which contained 5.25 per cent of nitrogen, of which 29.1 per cent was present in the form of the nitro group. The ease of nitration, together with the fact that the C:H

ratio of the nitration product of methylated lignin was nearly 1:1, indicated the aromatic character of the product (237).

Phelps (225) obtained a yellow dyestuff by the treatment of ligninsulfonic acid with nitric acid.

Nitro derivatives of ligninsulfonic acid from sulfite liquor were prepared by Oman (213) by the use of 50 per cent nitric acid at 30–40°C., or with mixed acid (1 part by weight of nitric acid and 1.5 parts by weight of concentrated sulfuric acid) at 30°C.

The nitration of ligninsulfonic acid has been reported by Dorée and Hall (37). One part of ligninsulfonic acid was heated on the water bath for 4 hours with 20 parts of 5 per cent nitric acid. The reaction product was dialyzed, and on evaporation a light orange-colored powder was obtained in 60 per cent yield. It was free from sulfur, and its composition could be represented by the formula $C_{25}H_{27}O_{17}N_2(OCH_3)$. When the nitration product was distilled with *N*/2 sodium hydroxide, 29 per cent of the nitrogen was evolved in the form of ammonia. The nitration product on reduction with zinc and hydrochloric acid yielded a nitrogen-free ketonic substance.

XII. SULFONATION (LIGNINSULFONIC ACIDS)

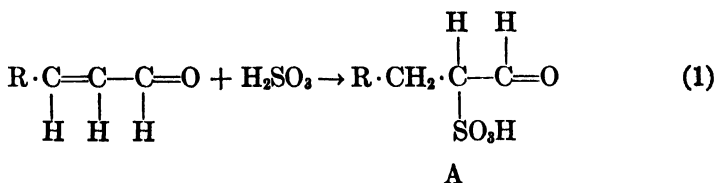
When wood and similar lignified materials are heated with a solution of sulfurous acid and acid sulfites, as in the sulfite process for pulping wood, the lignin goes into solution, leaving the cellulose in a more or less pure condition. The solution containing the lignin (waste sulfite liquor from pulp mills) has been the subject of numerous investigations. No attempt will be made here to review the extensive chemical and patent literature on the utilization of this industrial waste material. The résumé presented here includes only the important papers dealing with the chemistry of the lignin derivatives in the sulfite liquor.

Lindsey and Tollens (195) were the first to demonstrate that the lignin in waste sulfite liquor was present in the form of a calcium salt of a sulfonic acid, although this had previously been suggested by Pedersen (224). With lead acetate they obtained a precipitate from which the free acid could be obtained as an amorphous product. Analytical results agreed with the formula $C_{26}H_{30}SO_{12}$. This formula, according to Lindsey and Tollens, represented merely the average composition of the product and was not intended to indicate that they were dealing with a definite chemical compound. Later Streeb (276), working in Tollens' laboratory, found that the ligninsulfonic acids could be desulfonated by treatment with alkali.

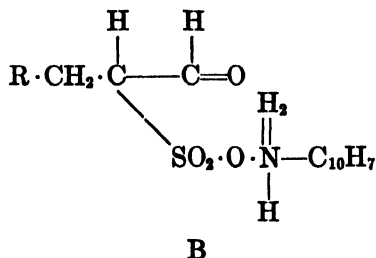
Hönig and Spitzer (140) attempted to obtain definite fractions from the ligninsulfonic acids. The ligninsulfonic acids were precipitated from

waste sulfite liquor with sulfuric acid, and the free sulfonic acids converted into their barium salts, which were then fractionally reprecipitated with alcohol. From the analytical data obtained from the several fractions of their barium salts, it was concluded that the ligninsulfonic acids were mixtures and not uniform substances. This has been confirmed by Melander (204) and by other investigators (171). Melander precipitated the ligninsulfonic acid from sulfite liquor with sodium chloride and found that only a portion of the total lignin derivatives present were thus precipitated. That fraction of the ligninsulfonic acids which could be precipitated with sodium chloride he designated α -lignin-S-acid, and that which could not thus be precipitated he designated β -lignin-S-acid. The former apparently differed materially from the α -ligninsulfonic acid of Klason.

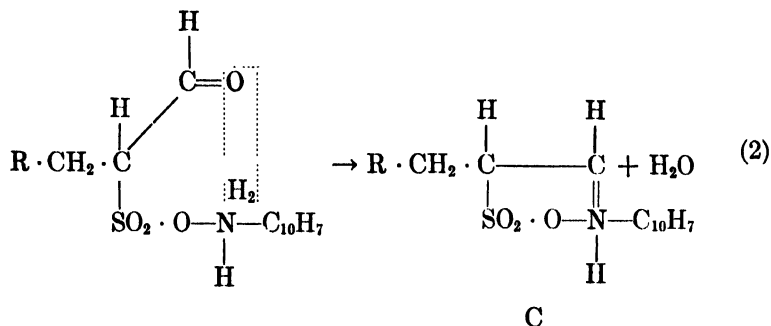
Klason (157) employed calcium chloride instead of sodium chloride for the precipitation of the ligninsulfonic acids, because the excess precipitant could be removed with alcohol. The fraction precipitated with this reagent Klason named α -ligninsulfonic acid, and that portion which remained in solution he designated β -ligninsulfonic acid. Subsequently it was found that β -naphthylamine hydrochloride was a much more desirable precipitant for α -ligninsulfonic acid (161). When the β -naphthylamine precipitate was warmed with dilute alkali it was found that only part of the β -naphthylamine could be split out. This, according to Klason, could be explained on the assumption that the lignin-fraction yielding α -ligninsulfonic acid contained the acrolein grouping. The first step in the reaction of the lignin with sulfurous acid, according to Klason, consisted in adding the elements of this acid as indicated in equation 1.



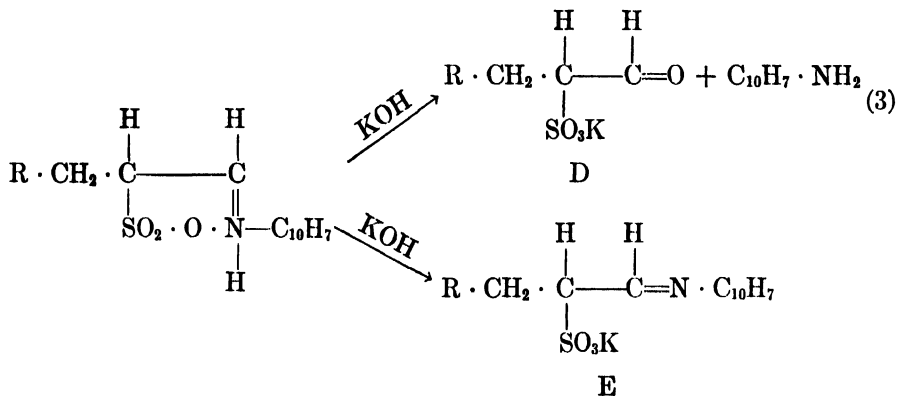
When the sulfonic acid (A) was treated with β -naphthylamine at first the normal salt (B) separated out as a white precipitate. A secondary reaction



then took place, and the yellow inner salt (C) was formed in a manner indicated in equation 2. When C was treated with alkali the reaction



proceeded in two ways as indicated below (equation 3).



Of the total ligninsulfonic acids in sulfite liquor approximately two-thirds was found to be in the form of the α -acid and one-third in the form of the β -acid. According to Klason β -ligninsulfonic acid contains an acrylic acid group.

Lignin, according to Klason, combines with four molecules of sulfur dioxide, only two of which are present in the form of the sulfonic acid. The third is more loosely combined, and although not titratable with iodine, gradually splits off as sulfuric acid on standing in contact with air. The fourth molecule is the most weakly combined and can be titrated with iodine.

Hintikka (133) questions whether an acrolein group is present in lignin which combines with sulfurous acid to form a soluble sulfonic acid.

Dorée and Hall (36) isolated a ligninsulfonic acid from the liquor obtained by heating spruce wood with 7 per cent sulfurous acid at 100–110°C.,

which resembled the α -ligninsulfonic acid of Klason. They were, however, unable to obtain evidence as to the formation of an inner salt of the type C and considered the β -naphthylamine precipitate a simple salt of the base with the sulfonic acid.

The evidence which Klason has presented as to the presence of acrolein and acrylic groups in α - and β -lignin, respectively, is rather fragmentary and incomplete, although some of the work of Hägglund (96) tends to support Klason's ideas. Klason's analytical data were obtained, of course, on amorphous material, and it cannot accordingly be stated definitely whether the α - and β -ligninsulfonic acids are really homogeneous substances. However, Klason's speculations on the structure of lignin and the mechanism of the reaction between lignin and sulfurous acid and bisulfites have stimulated research on this phase of lignin chemistry.

Hägglund (95) heated wood with a solution of sulfurous acid and bisulfite and at various intervals some of the liquor was withdrawn, and precipitated

TABLE 6
Composition of β -naphthylamine precipitate from sulfite liquor

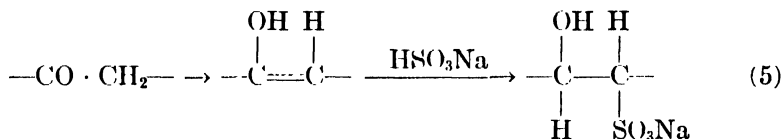
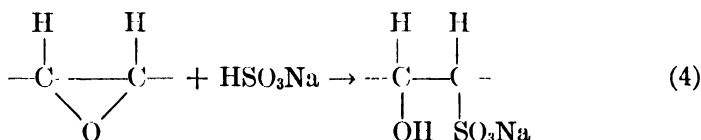
COLOR OF LIQUOR	HEATING PERIOD	CARBON	HYDROGEN	SULFUR	NITROGEN
	hours	per cent	per cent	per cent	per cent
Light yellow.	13	63.0	5.3	5.2	2.3
Yellow.	15	63.8	5.3	5.1	2.2
Brown.	17	62.8	5.0	5.3	2.25
Dark brown.	18	63.6	5.4	5.8	—
Black.	20	63.0	5.2	6.2	—

with β -naphthylamine hydrochloride. His analytical results are given in table 6, from which it will be observed that the first three precipitates had substantially the same elementary composition. When heating was continued longer than seventeen hours the composition of the product changed considerably, as is evident from the increase in the percentage of sulfur (table 6).

The solubility of Willstätter lignin in bisulfite solution varies considerably with the procedure followed in isolating the lignin. The longer the lignin remains in contact with the fuming hydrochloric acid, the more difficult it is to dissolve it in bisulfite solution. The sulfonation proceeds in two stages. In the first stage, an insoluble ligninsulfonic acid is formed, which in the presence of the cooking liquor is converted into soluble ligninsulfonic acids. The rate of dissolution of the lignin is directly related to the pH of the cooking liquor, so that in the presence of sulfurous acid the sulfonation of the lignin takes place faster than when sodium bisulfite solution alone is employed (101).

According to Hägglund (97) β -lignin is not preëxistent in pine wood, but β -ligninsulfonic acid is produced from the α -acid during the treatment with bisulfites at high temperatures. It is suggested that the diminution in the methoxyl content in the passage from the α - to the β -acid is due to an oxidizing action, since the methoxyl content of the α -acid was found to fall from 9.77 per cent to 6.14 per cent after treatment with 2 per cent hydrogen peroxide solution for 12 hours at ordinary temperature.

There is at present some disagreement among investigators as to the mechanism of the reaction between lignin and sulfurous acid and bisulfites. In order to account for the fact that fairly stable ligninsulfonic acids are formed, Klason (152) has assumed, as already stated, that the sulfurous acid is added at an ethylenic bond in the lignin molecule. Freudenberg (64), however, has recently come out in favor of the view that the sulfonic acid group is substituted in a benzene ring. According to Hägglund (100), when lignin is sulfonated there is formed one hydroxyl group for every unit of the lignin molecule containing two methoxyl and two hydroxyl groups. This, according to Hägglund, can best be explained on the assumption that an oxygen linkage between two carbon atoms is ruptured as indicated below (equation 4), or a ketone methylene group is rearranged to its enolic form, which then reacts with sulfurous acid or bisulfites as indicated in equation 5.



XIII. OXIDATION

The published results on the oxidation of lignin are rather disappointing in so far as throwing any light on the structure of this substance is concerned. When lignin is subjected to oxidation even under mild conditions, complete disruption of the molecule takes place and simple degradation products are obtained. König (173) ozonized Willstätter lignin suspended in water and in glacial acetic acid. Formic and oxalic acids were the oxidation products identified. Similar results were obtained when barium ligninsulfonate and ligninsulfonic acids were ozonized (36). The oxidation of lignin with hydrogen peroxide in neutral and in alkaline solutions as well

as the oxidation with potassium permanganate yielded simple organic acids, such as formic, acetic, oxalic, succinic, and malonic acids. Among those who have studied the oxidation of lignin and have obtained the above oxidation products may be mentioned König (174), König and Rump (183), Anderzén and Holmberg (1), Hägglund and Björkman (99), Urban (286), and Rassow and Zickmann (250).

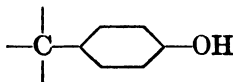
Fischer and Tropsch (49) heated lignin isolated by the fuming hydrochloric acid method with 10 *N* potassium hydroxide solution at 300°C., and obtained adipic acid. However, when the above experiment was conducted at 250°C. instead of at 300°C., oxalic and succinic acids were obtained but no adipic acid.

Fischer, Schrader, and Friedrich (48) subjected lignin to what these investigators designated as "pressure oxidation," which consisted essentially in heating lignin with 1.25 *N* sodium hydroxide solution in an autoclave at 200°C. under 55 atmospheres pressure, and obtained in addition to some simple aliphatic acids, such as formic, acetic, oxalic, succinic, and fumaric acids, small quantities of aromatic acids, such as benzoic (0.6 per cent), phthalic (trace), isophthalic (0.05 per cent), trimellitic (0.5 per cent), hemimellitic (0.53 per cent), prehnitic (0.12 per cent), pyromellitic (0.28 per cent), benzene pentacarboxylic (1.65 per cent), and mellitic (0.38 per cent) acids. However, in view of the rather drastic method of oxidation employed by Fischer and coworkers, it seems doubtful whether their results can be interpreted as definitely indicating that an aromatic nucleus is present in the lignin molecule.

Previous methylation of the lignin and the subsequent oxidation with potassium permanganate failed to alter the course of the reaction, oxalic acid being the only oxidation product obtained (120). The same reaction product was obtained when lignin was oxidized with hydrogen peroxide (119) and with nitrogen tetroxide (258). Drastic oxidation of lignin with nitric acid afforded oxalic and mellitic acids (142).

In a patent application, Pauly and Feuerstein (221) claimed that lignin or lignin-containing substances when oxidized with ozone in glacial acetic acid yield vanillin. Other oxidizing agents which may be employed are chromic acid in glacial acetic acid, potassium permanganate, and activated oxygen. This work requires confirmation.

Phillips and Goss (237) found that alkali lignin from corn cobs when oxidized with ozone yielded oxalic acid. However, when the lignin was first methylated and then oxidized with 5 *N* nitric acid or with ozone, anisic acid was obtained. When lignin was ethylated and then oxidized, *p*-ethoxybenzoic acid was obtained. This indicates that the group



is in all probability present in alkali lignin from corn cobs and that the methyl group of the anisic acid represented one which had been introduced by the methylation process and not one which was naturally present in lignin. In the oxidation of methylated lignin with the 5 *N* nitric acid, there was obtained, in addition to the anisic acid, an orange-colored amorphous product containing 5.25 per cent of nitrogen, of which 29.1 per cent was present in the form of the nitro group. The ease of nitration, together with the fact that the C:H ratio of the nitrated methyl lignin was found to be nearly 1:1, tended to indicate the presence of an aromatic nucleus in the alkali lignin from corn cobs.

XIV. REDUCTION

Reduction with hydriodic acid and phosphorus

Willstätter and Kalb (300) heated lignin isolated by the fuming hydrochloric acid method with hydriodic acid and red phosphorus at 250°C. The reaction product consisted of a mixture of hydrocarbons together with some oxygen-containing substances of an acidic nature. The hydrocarbons were resolved into an acetone-soluble or liquid fraction and an acetone-insoluble or solid fraction. The former contained 88.14 per cent of carbon and 11.85 per cent of hydrogen. The molecular weight ranged from 167 for the lowest liquid fraction to 842 for the highest solid fraction. No definite compound was separated. It was established that *n*-hexyl iodide was not an intermediate product. Mixtures of hydrocarbons of the same general composition were obtained by the reduction of cellulose, glucose, and other carbohydrates. This, according to Willstätter and Kalb, indicates that a close structural relationship exists between lignin and the carbohydrates. In view of the rather drastic method of reduction employed, however, it seems rather doubtful whether any such definite conclusion is justified.

Catalytic hydrogenation under pressure

Fierz-David and Hannig (44) subjected Willstätter lignin to catalytic hydrogenation under a pressure of 250 atmospheres, nickel being used as the catalyst. The distillation products from 500 g. of lignin are given in table 7. The tar contained 39.0 g. of phenols and 21.5 g. of neutral substances. In the absence of the nickel catalyst practically no hydrogenation took place even at 300 atmospheres pressure.

Bowen and Nash (10) gradually heated lignin to about 450°C. with hydrogen under pressure (maximum up to 240 atmospheres) in the presence of catalysts, such as alumina and nickel oxide. Liquid and gaseous products were formed, but the oils obtained were not fully saturated, owing

probably to the deposition of small quantities of coke on the catalyst. The oil contained phenolic substances.

Zinc dust distillation

Karrer and Boddington (150) heated Willstätter lignin with zinc dust in an atmosphere of hydrogen. None of the fractions was oxygen-free, nor did they appear to be homogeneous. From one fraction a crystalline substance melting at 210–212°C. was separated, but the identity of it was not established.

Phillips (232) distilled alkali lignin isolated from corn cobs with zinc dust in an atmosphere of hydrogen at a temperature not exceeding 400°C. The aqueous distillate contained catechol. An oil was obtained equal to 16 per cent of the weight of the lignin used. In the phenolic fraction of the oil, guaiacol and 1-*n*-propyl-3-methoxy-4-hydroxybenzene were identified. The "neutral" fraction of the oil when oxidized with potassium permanga-

TABLE 7
Products from catalytic hydrogenation of lignin

PRODUCTS	QUANTITY
	<i>grams</i>
Combustible residue	78.0
Aqueous distillate	251.0
Tar	89.0
Ash, and gaseous products	88.0

nate yielded anisic acid. The isolation of these degradation products of lignin indicates that there are in the lignin molecule, in addition to other possible units, at least two aromatic nuclei or those which can be readily converted into aromatic nuclei. One nucleus has a side chain having at least three carbon atoms in addition to a methoxyl group and a hydroxyl group in the positions meta and para, respectively, to the side chain. The other nucleus has a side chain and a methoxyl substituent para to the side chain.

XV. HYDROLYSIS

The demethoxylation of lignin by heating it with dilute acids under pressure has been reported by Heuser (121) and coworkers. Ten grams of lignin was heated for 3.5 hours in a sealed tube at 150–160°C. with 100 cc. of 5 per cent hydrochloric acid. The lignin lost practically none of its methoxyl by this treatment. However, when this operation was repeated for three times at a temperature of 170–180°C. complete demethoxylation resulted. In addition, deep-seated changes in the composition of the

lignin took place, for the demethoxylated product could only be partly methylated with dimethyl sulfate. After three successive treatments with this methylating agent a dark product was obtained which contained only 5.79 per cent of methoxyl.

Holmberg and Wintzell (137) and Beckmann, Liesche, and Lehmann (5) heated lignin with hydriodic acid and obtained dark colored amorphous products soluble in alkali. The last-named investigators heated lignin, which had been isolated from winter-rye straw by the alcoholic sodium hydroxide method, with hydriodic acid (d. 1.9) in glacial acetic acid solution for 4 hours. The product was completely demethoxylated and contained chemically bound iodine.

Hägglund (93) hydrolyzed lignin which he prepared from spruce by his method (hydrolysis of the wood for 15 minutes with 45 per cent hydrochloric acid at 0°C.) with fresh portions of boiling 3 per cent hydrochloric acid until the acid extract gave no test for sugar with Fehling's solution. In this operation 33.7 per cent of the starting material was lost, and the acid extract contained 15.8 per cent of sugar. With *p*-bromophenylhydrazine a hydrazone melting at 155°C. was obtained. The sugar was therefore, in all probability, arabinose. Hägglund considered the carbohydrate as part of the structural arrangement of the lignin molecule. This seems doubtful, and as Heuser (113) has pointed out, the presence of pentosans or pentoses in lignin preparations can be ascribed to incomplete hydrolysis of the lignified plant material. In this connection, it may be pointed out that the lignin isolated from wood with alkali by Powell and Whittaker (243) and the lignin fraction isolated by Phillips (226) from corn cobs were entirely free from furfural-yielding substances.

Hägglund and Björkman (98) and later Hägglund and Rosenqvist (104) distilled Willstätter lignin with 12 per cent hydrochloric acid and obtained a distillate which gave a precipitate with phloroglucinol, barbituric acid, and thiobarbituric acid. The substance present in the distillate was not definitely identified, but was shown to be neither furfural, methylfurfural, nor hydroxymethylfurfural. This substance was subsequently identified by Freudenberg and Harder (58) as formaldehyde. The significance of the identification of formaldehyde as a fission-product of lignin from the standpoint of the presence of the methylene dioxide group in lignin is discussed elsewhere.

Aronovsky and Gortner (2) found when wood was heated with water under pressure that although the total quantity of lignin as determined by the 72 per cent sulfuric acid method remained practically constant, part of the lignin was altered so as to be soluble in alcohol, indicating that possibly depolymerization had taken place.

When barium ligninsulfonate was refluxed for 4 to 6 hours with a satu-

rated solution of barium hydroxide, a portion of the lignin derivatives dissolved. From this solution a light yellow amorphous product was obtained which in many of its properties resembled tannins. It gave a greenish coloration with ferric chloride solution, and was precipitated with solutions of lead acetate, quinine hydrochloride, and gelatin. It was furthermore absorbed by hide powder and had an astringent taste. The composition of the free acid could be represented by the formula $C_{18}H_{32}O_{10}S$. On fusion with potassium hydroxide protocatechuic acid was obtained (139).

XVI. FUSION WITH ALKALIES

The fusion of lignin with alkali has been undertaken by several investigators. The reaction products in nearly all cases have been protocatechuic acid, catechol, oxalic, and other simple aliphatic acids. Vanillic acid has also been reported as one of the degradation products. In addition to the above substances, there is always obtained a dark, amorphous, humin-like degradation product generally referred to as "lignic acid." Below $240^{\circ}C$., the main product of the fusion is "lignic acid."

Fischer and Tropsch (49) fused Willstätter lignin with potassium hydroxide at 240 – $300^{\circ}C$. There was obtained 35.5 per cent of humin-like material and 14.9 per cent of ether-soluble substances. In the latter, protocatechuic acid was identified. There was also isolated a crystalline substance which did not melt below $260^{\circ}C$. and which gave a green coloration with ferric chloride. The identity of this substance was not established.

Among others who have identified protocatechuic acid in the alkaline melt of lignin may be mentioned Klason (160), Hägglund (91), and Hägglund and Malm (103).

Heuser and coworkers have made extensive studies of the fusion of lignin with alkali. It was first reported that protocatechuic acid, but no oxalic acid, was formed by the fusion of carbohydrate-free lignin with potassium hydroxide at a maximum temperature of $270^{\circ}C$. (117). It was later (125) found, however, that a 20 per cent yield of oxalic acid could be obtained when 4 parts of lignin and 50 parts of potassium hydroxide were heated for 40 minutes at $280^{\circ}C$.

Heuser and Winsvold (126) fused lignin with 10 parts by weight of potassium hydroxide and 2 to 3 parts of water at 240 – $290^{\circ}C$. for $\frac{1}{2}$ to $1\frac{1}{2}$ hours. Various substantial amounts of "lignic acid" were recovered from the product of the fusion. The aromatic products obtained consisted of protocatechuic acid (16 to 19 per cent) and catechol (1 to 3 per cent). When the fusion was conducted in contact with air, secondary oxidation

took place, with the formation of oxalic acid (up to 20 per cent). However, when the fusion was carried out in an atmosphere of hydrogen or nitrogen, the formation of oxalic acid was practically suppressed and the yield of catechol increased to 9 per cent. Iron appears to have considerable influence on the course of the reaction. The fusion of lignin with alkali in an iron crucible out of contact with air increased the yield of catechol up to 23 per cent, but the presence of protocatechuic acid could no longer be detected. Protocatechuic acid appears to be the primary product of the reaction; the catechol is formed from it by the elimination of carbon dioxide. This finds confirmation in the fact that when Heuser and Winsvold fused pure protocatechuic acid with potassium hydroxide in the presence of air, the yields of catechol and oxalic acid were 2.5 and 20 per cent, respectively. When the fusion was conducted in an atmosphere of hydrogen, no oxalic acid was obtained, and the yield of catechol increased to 19 per cent and could be increased to 26 per cent when iron was present in the melt.

The fact that substantial amounts of aromatic substances are formed in the alkali fusion of lignin is seen by Heuser and Winsvold as additional evidence in favor of the hypothesis that lignin contains a benzenoid nucleus. Under similar conditions, cellulose yields only negligible quantities of aromatic derivatives.

When iron powder is present in the alkali fusion mixture, the yield of aromatic substances obtainable from lignin is increased, and the elimination of carbon dioxide from protocatechuic acid is promoted, but not to such a large extent as when the fusion is performed in an iron crucible. There is only a slightly lower yield when the fusion is carried out at 240–260°C. instead of 270–280°C. Fusion in an atmosphere of carbon dioxide exerts a protective influence in suppressing the formation of oxalic acid, but not so completely as hydrogen. Carbon dioxide also moderates the total reaction and more "lignic acid" is obtained. Carbon dioxide is produced to the extent of 27 to 28 per cent of the weight of the lignin when the fusion is carried out in a nickel crucible in the presence of air. Since the decomposition of protocatechuic acid into catechol is only promoted in the presence of an iron catalyst in an atmosphere of hydrogen, the carbon dioxide formed under normal conditions is the result of oxidation of other products of the reaction (116).

The fusion of 3 parts of lignin with the 20 parts of potassium hydroxide, 20 parts of water and 12 parts of zinc dust at 250°C. for 1½ hours afforded a yield of protocatechuic acid which varied from 7 to 15 per cent (250).

The methylation of lignin and subsequent fusion of the methylated product with potassium hydroxide at 270–280°C. had little effect on the character and yield of aromatic substances obtained (286).

Freudenberg, Harder, and Markert (60) obtained only a 4.8 per cent yield of protocathechuic acid (isolated as its dimethyl ether—veratric acid) when technical lignin was fused with potassium hydroxide at 260–270°C. in an atmosphere of nitrogen. When pure protocathechuic acid was subjected to fusion with potassium hydroxide under similar conditions, about one-half of the acid was lost in this treatment. Because of this, Freudenberg, Harder, and Markert feel justified in stating that the yield of protocathechuic acid obtained is only one-half of that actually formed and probably amounts to from 9 to 10 per cent.

Beckmann, Liesche, and Lehmann (5) have shown that the yields of phenols and protocathechuic acid obtainable in the alkali fusion of lignin from straw depend considerably on the method used for isolating the lignin, as can be seen from table 8.

Holmberg and Wintzell (137) isolated a lignin fraction from so-called black liquor (a waste product obtained in the delignification of wood by the sodium hydroxide process) and subjected this to fusion with potassium

TABLE 8
Products of the alkali fusion of lignin from straw

PRODUCTS	METHOD USED FOR ISOLATING LIGNIN		
	Cold NaOH	Reflux with NaOH	NaOH in CH_3OH
Protocatechuic acid.....	6.0 to 7.6 per cent	7.0 to 8.0 per cent	15.3 per cent
Phenols.....	2.2 to 3.3 per cent	0.6 to 1.5 per cent	45.0 per cent

hydroxide. They obtained protocathechuic acid together with some oxalic and acetic acids.

The alkali fusion of the so-called ligninsulfonic acid obtainable from waste sulfite liquor has received the attention of several investigators. Melander (203) obtained catechol, protocathechuic acid, vanillic acid, acetic acid, and traces of higher fatty acids. The yield of catechol amounted to 10 per cent of the organic portion of the starting material.

Hönig and Fuchs (138) subjected to alkali fusions the fractions of barium ligninsulfonate prepared according to the method of Hönig and Spitzer (140). Two grams of barium lignin sulfonate, 8 g. of potassium hydroxide, and 8 cc. of water were heated in a nickel crucible at 240–250°C. The temperature was gradually raised to 300°C. and kept at this point not longer than 10 minutes. The yield of protocathechuic acid varied from 13 to 19 per cent, based on the organic portion of the starting material. Although a positive test for catechol with ferric chloride was obtained, this compound was, however, not actually isolated.

XVII. DRY DISTILLATION

Hägglund (90) distilled lignin isolated from pine wood by the hydrochloric acid method of Willstätter and Zechmeister and obtained 45 per cent carbon residue, 9.6 per cent oil, 0.10 per cent acetone, 0.67 per cent methanol, and 0.64 per cent acetic acid.

Fischer and Schrader (47) distilled Willstätter lignin and obtained 13.2 per cent aqueous distillate, 12.5 per cent oil, 57.2 per cent carbon residue, and 17.0 per cent gas (obtained by difference). It was found that 16.4 per cent of the oil dissolved in sodium carbonate and 33.9 per cent in sodium hydroxide solutions.

Tropsch (283) destructively distilled commercial Willstätter lignin under reduced pressure (1 to 2 mm.) and obtained 14.2 per cent aqueous distillate, 10.2 per cent oil, and 53.8 per cent carbon residue. The oil contained 37.5 per cent phenolic compounds. Results of a similar character were obtained by Fischer and Tropsch (51).

Pictet and Gaulis (240) distilled technical Willstätter lignin under reduced pressure. The temperature varied from 350°C. to 390°C., and the pressure from 5 to 25 mm. The lignin yielded 15 per cent of its weight in oil, 21 per cent aqueous distillate, and 52 per cent carbon residue. No examination of the aqueous distillate was made. The oil was extracted with 10 per cent sodium hydroxide solution, in which 89 per cent dissolved. In the alkali-soluble fraction eugenol was identified. The alkali-insoluble fraction was separated by means of liquid sulfur dioxide into saturated and unsaturated hydrocarbons. They consisted entirely of hydroaromatic hydrocarbons. The saturated hydrocarbons gave five fractions having approximately the following compositions: 235–240°C., $C_{13}H_{26}$; 260–270°C., $C_{14}H_{28}$; 270–280°C., $C_{16}H_{30}$; 315–320°C., $C_{24}H_{44}$; above 320°C., $C_{30}H_{60}$. In the last fraction melene, a hydrocarbon found in some coal tars and in Galician petroleum, was identified. The unsaturated hydrocarbons gave three fractions, 200–210°C., $C_{11}H_{16}$; 230–240°C., $C_{12}H_{16}$; 250–260°C., $C_{13}H_{16}$. Of these, the first appeared to be identical with a coal tar fraction. The last fraction gave a tetrabromo derivative, $C_{13}H_{12}Br_4$, which melted at 193°C. and appeared to be related to hexahydrofluorene of coal tar. Pictet and Gaulis believe that their results indicate a relationship between lignin tar and coal tar, and to that extent support the hypothesis of Fischer and Schrader (46) that coal originated not from the cellulose of the plants but rather from the lignin. The isolation of eugenol they believe confirms the view that lignin contains the grouping of coniferyl alcohol. The results also indicate the existence of a hydroaromatic ring in lignin. It must be remembered, however, that the degradation products referred to were obtained by subjecting lignin to a very drastic treatment and results

obtained by such methods must necessarily be interpreted with considerable reserve.

Kürschner (189) subjected lignin to what he calls sublimation, but it is not sublimation in the ordinary sense of the term but rather a thermal degradation of lignin. Small quantities of lignin were heated to 200°C. in a special apparatus, and crystals of vanillic acid were obtained.

Heuser and Brötz (115) distilled lignin isolated by the fuming hydrochloric acid method from pine and aspen following the method used by one of the authors in a previous investigation (124), and the results obtained were respectively as follows: carbonized residue, 45.6 and 44.3 per cent; tar, 13.3 and 14.2 per cent; aqueous distillate, 29.7 and 30.5 per cent; acetic acid, 1.26 and 1.28 per cent; methanol, 0.82 and 0.86 per cent; acetone, 0.18 and 0.21 per cent.

Dry distillation of a mixture of technical Willstätter lignin and silver powder at 280–300°C. gave about 10 per cent of distillate consisting of an aqueous and a tarry layer (75). The former contained catechol to the extent of 0.5 per cent of the original lignin, a little guaiacol, an organic acid, and 5-hydroxymethylfurfural. In the tarry distillate eugenol and melenene were identified. Similar results were obtained by treating technical Willstätter lignin with superheated steam at 280–300°C. Consideration of the yield of 5-hydroxymethylfurfural, Fuchs believes, indicates the presence of a hexal but not a hexose complex in lignin (76).

Szelenyi and Gömöry (280) distilled lignin isolated from beech, oak, and birch. The yields of aqueous distillates and tar were about the same in all cases, namely, 19 and 3 to 4 per cent, respectively. Of the total percentage of methoxyl in oak lignin and beechwood lignin, about 10 per cent was accounted for in the distillate, whereas in the case of birch lignin, only 7.9 per cent was thus accounted for.

Phillips (228) made a study of the dry distillation of lignin from corn cobs isolated by three different methods, namely, the alkali method, the fuming hydrochloric acid method of Willstätter and Zechmeister, and the 72 per cent sulfuric acid method. From the alkali lignin the following results were obtained: aqueous distillate, 15.5 per cent; water-insoluble oily distillate, 17.7 per cent; carbon residue, 52.2 per cent; gas (by difference), 13.5 per cent; acetone, 0.13 per cent; methanol, 1.9 per cent; acids (calculated as acetic acid), 0.05 per cent. The oily distillate analyzed as follows (the results are expressed as per cent by weight of the oil): acids, 8.6 per cent; phenols, 84.0 per cent; neutral substances, 7.2 per cent. In the case of the Willstätter lignin and the lignin prepared by the 72 per cent sulfuric acid method, the percentage of aqueous distillate was about the same as that obtained from alkali lignin, whereas the oily distillate was only about one-half. The percentages of carbon residue obtained from the Will-

stätter lignin and from the 72 per cent sulfuric acid lignin were considerably greater than that obtained from alkali lignin. The percentages of acetone and acetic acid obtained were considerably greater in the case of the Willstätter and the 72 per cent sulfuric acid lignin than in the alkali lignin, whereas the percentage of methanol was less. This higher percentage of methanol is probably due in part to the greater methoxyl content of alkali lignin as compared with that of Willstätter and 72 per cent sulfuric acid lignin. The low yield of acetic acid obtained from alkali lignin is explained by the fact that in preparing lignin by this method deacetylation occurs.

In a subsequent paper Phillips and Goss (235) reported the results of a systematic chemical examination of both the aqueous and oily distillates

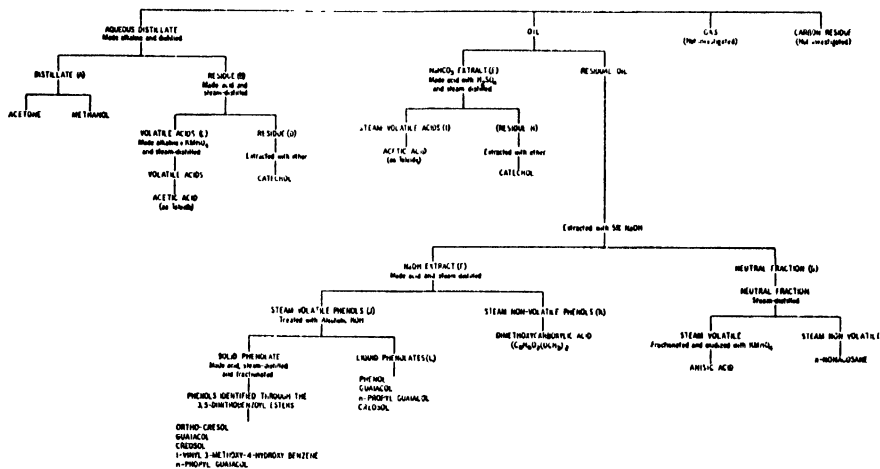


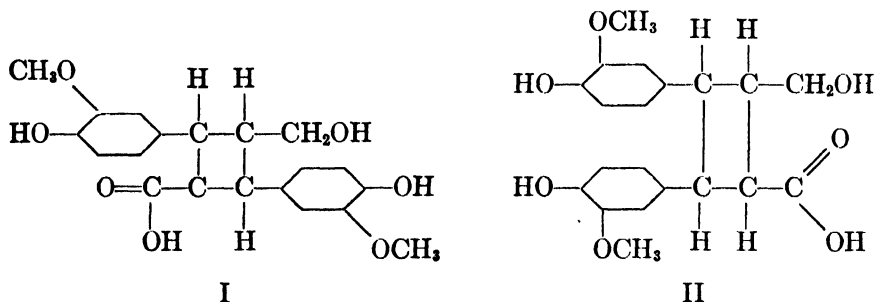
FIG. 1. PRODUCTS OBTAINED IN THE DRY DISTILLATION OF LIGNIN IN A REDUCED ATMOSPHERE OF CARBON DIOXIDE

obtained when alkali lignin from corn cobs was subjected to dry distillation at a reduced atmosphere (25 mm.) of carbon dioxide. The following results (calculated on the basis of dry lignin) were obtained: aqueous distillate, 11.7 per cent; oily distillate, 28.3 per cent; carbonized residue, 50.5 per cent; gas (by difference), 9.3 per cent. The aqueous distillate contained acetic acid, acetone, and methanol, in amounts of (calculated on the basis of dry lignin) 0.30, 0.10, and 0.65 per cent, respectively. Catechol was identified in the aqueous distillate. In the oil the following compounds were identified: acetic acid, catechol, phenol, *o*-cresol, guaiacol, creosol, 1-vinyl-3-methoxy-4-hydroxybenzene, 1-*n*-propyl-3-methoxy-4-hydroxybenzene, and a dimethoxycarboxylic acid, $C_6H_4O_2 \cdot (OCH_3)_2$. The steam-volatile "neutral" fraction of the oil, when oxidized with potassium permanganate, yielded anisic acid. In the non-steam-volatile "neutral"

fraction of the oil, *n*-nonacosane was identified. The results of this investigation are given schematically in figure 1.

XVIII. THEORIES CONCERNING THE CONSTITUTION OF LIGNIN

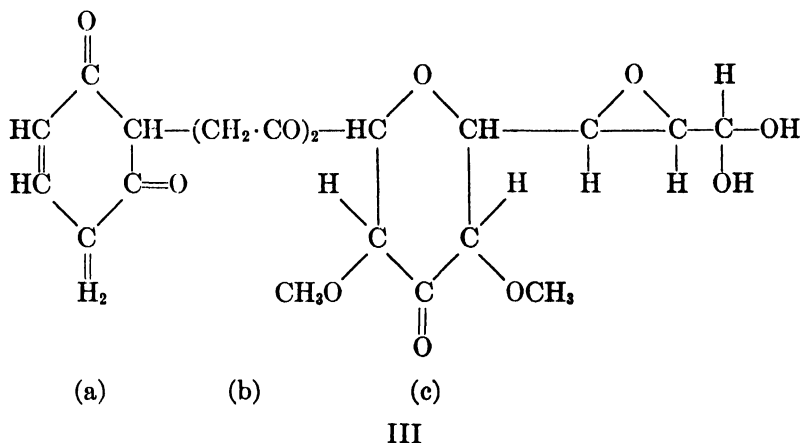
Considerable difference of opinion prevails among investigators of the chemistry of lignin as to whether this substance belongs to the aliphatic, aromatic, hydroaromatic, or heterocyclic series. Willstätter and Kalb (300), as a result of their work on the reduction of lignin with hydriodic acid and red phosphorus, have concluded that lignin is structurally related to the carbohydrates. They based their conclusion on the fact that similar reduction products were obtained from lignin and from certain carbohydrates. However, none of the products they obtained was homogeneous. They were unable to identify any definite chemical substance. Jonas (146) and Marcusson (198) contend that lignin is not aromatic but is made up of furane nuclei, but very little definite experimental evidence has been presented in support of this. However, the evidence obtained from the experiments on the alkali fusion, zinc dust distillation, dry distillation, "sublimation," oxidation, halogenation, nitration, and metabolism of lignin, when taken all together, indicates that lignin contains either an aromatic nucleus or one which is readily converted into an aromatic nucleus (hydroaromatic). In this connection it may be pointed out that Holmberg (135) isolated a crystalline substance from waste sulfite liquor (a by-product from the delignification of wood by the sulfite process) in 0.1 to 0.2 per cent yield. This substance was found to be phenolic and contained two methoxyl groups, two hydroxyl groups that could either be acetylated or methylated, and a lactone group. On the basis of his experiments, Holmberg assigned either formula I or formula II to the hydroxy acid from which the lactone is derived. According to him, it may be considered as the inner anhydride of diguaiacoltetramethylenecarbinol



carboxylic acid. It may be stated, however, that the connection between this lactone and the original lignin in the wood has not yet been definitely established.

The literature concerning the structure of lignin is now rather extensive and quite a number of constitutional formulas have been proposed. It may be stated at the very outset that all these formulas are more or less speculative in character, although evidence of a fragmentary character can be mustered for their support. The fact that at frequent intervals the proponents of the constitutional formulas have themselves found it necessary to change them is in itself an indication of the very insecure foundation upon which they rest. However, since these speculative and tentative constitutional formulas have stimulated research on lignin, a brief résumé of the literature concerning them is here presented.

Cross and Bevan (23), as a result of their work on "lignone chloride," have proposed the following constitutional formula (III) for lignin:

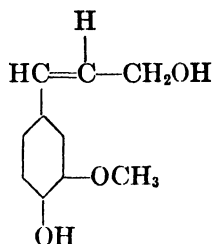


According to Cross and Bevan, chlorination takes place at the ethylenic bond of group (a), from which the derivatives of pyrogallol are subsequently obtained. However, it must be pointed out that attempts by other investigators to isolate these derivatives have always resulted in failure. The occurrence of the hydroprone group (c) is based on the fact that acetone and maltol were obtained at higher temperatures. Inasmuch as these fission products can be obtained from substances other than those having a hydroprone nucleus, this evidence is not valid. The presence of the group (b) is assumed because on hydrolysis, oxidation, and dry distillation, acetic acid is obtained. In view of the fact that this acid can be obtained from numerous organic substances, this evidence is not convincing.

A formula for lignin has been proposed by Green (88), but as it is no longer in harmony with our present knowledge of the chemistry of lignin, it need not be presented here.

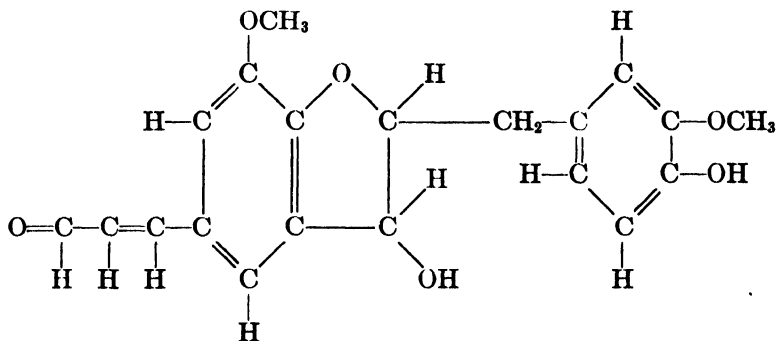
Klason was the first to suggest an aromatic structure for lignin. Accord-

ing to his original conception (153), lignin is a condensation product of coniferyl alcohol (IV) and oxyconiferyl alcohol. In view of the fact that

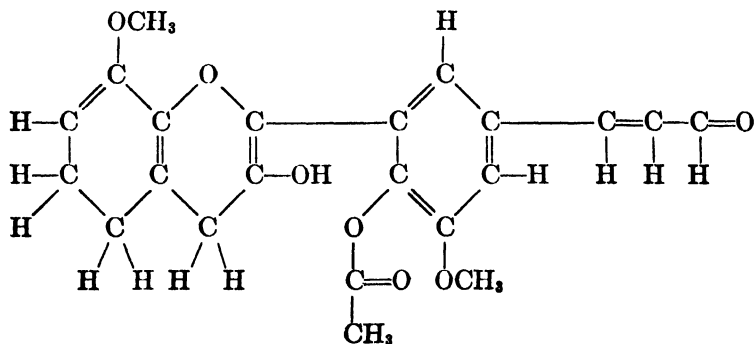


IV

he was subsequently able to isolate two lignosulfonic acids, one of which could be precipitated with calcium chloride and one which could not, Klason was led to the conclusion that there were two lignins. The lignin, the sulfonic acid of which was precipitated with calcium chloride, was designated α -lignin, and the other β -lignin. α -Lignin was considered a condensation product derived from coniferyl aldehyde and the following possible formulas (V and VI) were proposed for it (164):

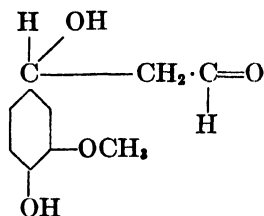


V



VI

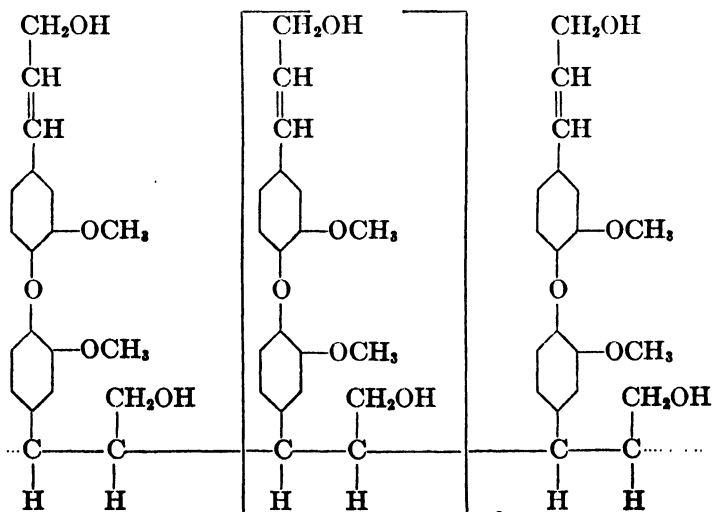
In subsequent publications (168) Klason found it necessary to alter considerably his conception as to the structure of lignin, and in a more recent article (169) he expresses himself in favor of the view that lignin contains the grouping represented by formula VII:



VII

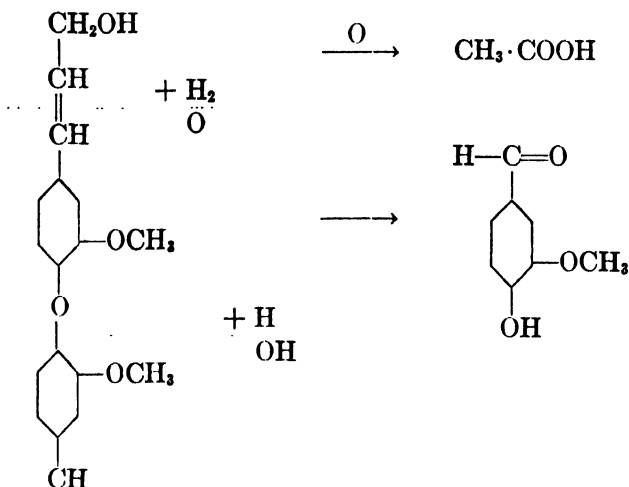
Whether lignin contains a grouping related to coniferyl alcohol or aldehyde has not been definitely established, although the results of experiments on dry distillation and zinc dust distillation of lignin would tend to support this hypothesis.

Kürschner (188) has advanced the hypothesis that lignin is a polymer of the glucoside coniferin, which Tiemann and Haarmann (281) have shown yields glucose and coniferyl alcohol upon hydrolysis. In support of this hypothesis, he points out the fact that he was able to obtain fairly large yields of vanillic acid in his "sublimation" experiments, and indicates further that coniferin and spruce lignin show an analogous behavior in several chemical reactions, such as action with sulfurous acid and bisulfites, fusion with alkalis, and solubility in trichloroacetic acid. In a recent article Kürschner (191) suggested the following as a possible structural formula for lignin (VIII):



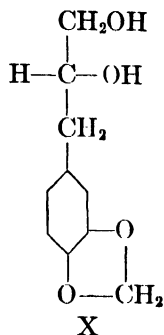
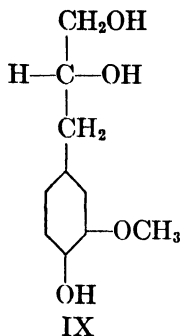
VIII

A compound of this formula could yield vanillin through a process of oxidation and hydrolysis, the vanillic acid resulting as a secondary oxidation product of the vanillin.

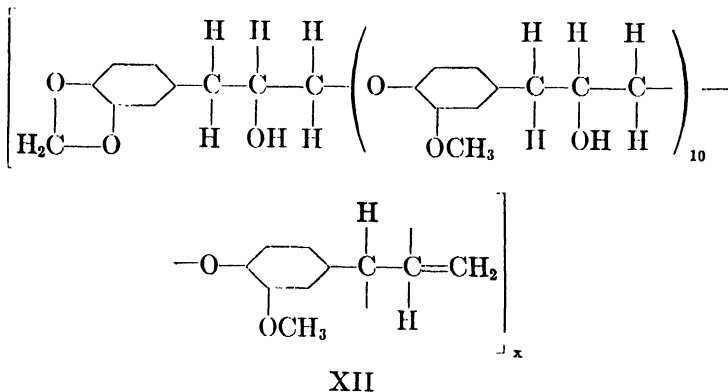
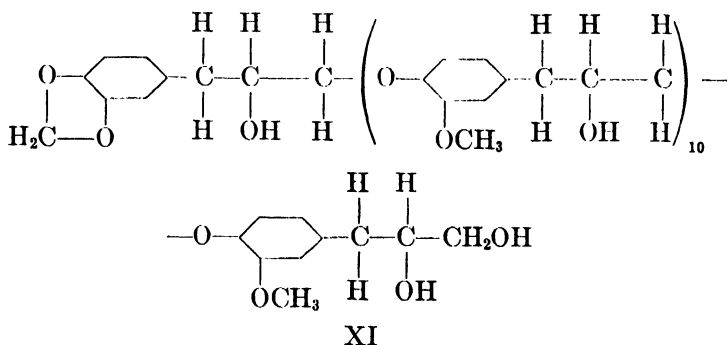


The fact that lignin does not behave like a true unsaturated compound would speak against the Kürschner conception of the structure of lignin. Further, when lignin is heated with hydriodic acid as in the Zeisel determination of alkoxyl groups, methyl iodide only is given off. This has been definitely established in the case of spruce lignin (105). If lignin were a derivative of coniferyl alcohol, one ought to obtain a mixture of methyl iodide and ethyl iodide upon heating it with hydriodic acid. Tiemann and Haarmann (281) have shown that coniferyl alcohol when heated with hydriodic acid gives both methyl iodide and ethyl iodide, the latter resulting from a degradation of the propylene side chain. In the Kürschner formula the various benzene nuclei are connected through oxygen in ether-like combination. A compound having such a structure ought to yield fairly simple derivatives of benzene when heated with hydriodic or hydrochloric acid. No such derivatives have been obtained from spruce lignin when treated in this manner.

A somewhat related theory has been put forth by Freudenberg (54). This investigator considers that the following two groups (IX and X) are the basic units from which lignin may be considered as derived. He assumes that the primary hydroxyl is joined through an ether linkage with one of the phenol hydroxyls of the next molecule and a condensation product represented by formula XI is formed. The material represented



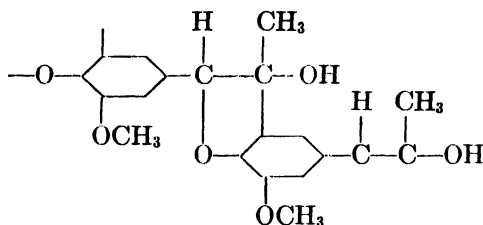
by formula XI Freudenberg calls "primary lignin." By the polymerization of "primary lignin" (XI) "secondary lignin" (XII) results.



This is formed either by condensation in the wood after the cells are dead or during the process of isolation in the laboratory. It is the parent substance of almost all lignin derivatives, particularly of ligninsulfonic acid. The latter substance is a result of partial elimination of water and addition of $\text{H}-\text{SO}_3\text{H}$ to the resulting double bond.

According to Freudenberg, the formulas XI and XII fulfill the following essential conditions which experiment requires: The formation of "primary lignin" in physiological synthesis from definite structural units; post mortem condensation of "primary lignin" to the three-dimensional "secondary lignin" of enormous molecular weight; the absence of phenolic hydroxyls; the presence of aromatic methoxyl, dioxymethylene, and secondary hydroxyl groups in the proportions indicated by the formula; the completely amorphous condition; the permutoid nature of the material, shown by the stoichiometric relations upon methylation or acetylation of the carbinol, or upon bromination, nitration, or mercuration of the nucleus. The refractive index, 1.61, also corresponds to this conception.

In a recent publication, Freudenberg (64) appears to have abandoned his original idea that the nuclei are joined together through an ether linkage, and suggests that union may take place as indicated in formula XIII:

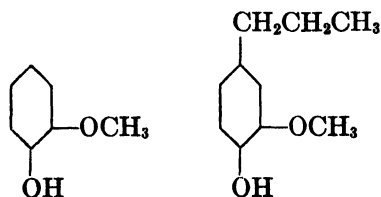


XIII

The ligninsulfonic acids are formed through a substitution in the benzene ring and do not result from the addition of the elements of H_2SO_3 at a double bond.

Although the formulas for lignin proposed by Freudenberg are still to a considerable extent speculative, yet it must be stated that he has mustered more facts in support of his ideas than any other investigator who has put forward a tentative constitutional formula for lignin. Freudenberg's ingenious speculations ought to prove useful and serve as stimuli to those engaged in the chemical investigations on lignin.

Phillips (231) isolated guaiacol (XIV) and *n*-propylguaiacol (XV) from the oil obtained in the distillation of lignin with zinc dust in an atmosphere of hydrogen, and has accordingly suggested that in all probability the two

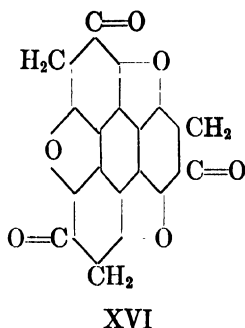


XIV

XV

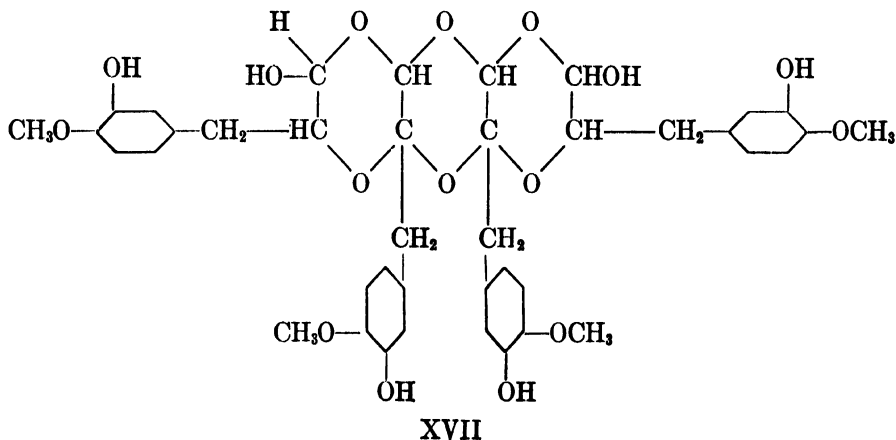
fundamental units in the structure of lignin are guaiacol and *n*-propyl-guaiacol, the latter having the hydrogen atoms in the *n*-propyl side chain substituted by hydroxyl groups. It may be pointed out in this connection that the ultra-violet absorption spectra of lignin and lignin derivatives, as determined by Herzog, Hillmer, and others (112), indicate a benzenoid structure for lignin. The absorption spectra of lignin preparations resemble those of coniferyl alcohol and related compounds.

Schrauth (263) has proposed a constitutional formula for lignin. This formula (XVI) is admittedly speculative.



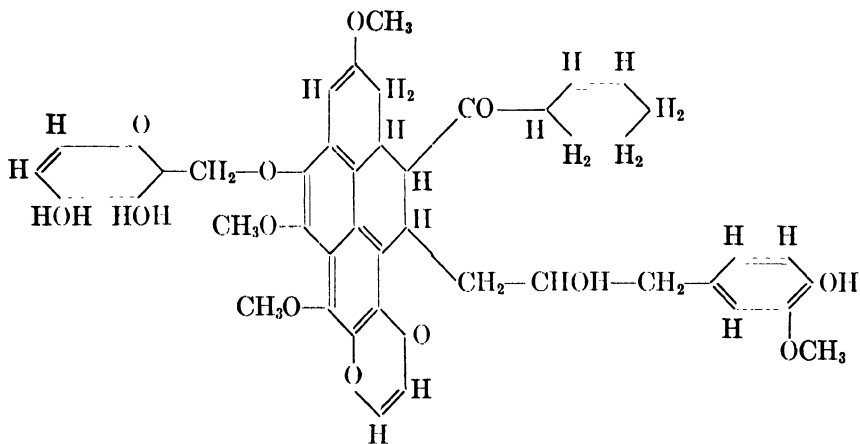
It is suggested that the fundamental unit of the lignin molecule is formed by the condensation of three molecules of 5-hydroxymethylfurfural, which is itself produced by the internal condensation of carbohydrates. Units so formed consist of a compact condensed ring system, of which three of the outer rings are furane nuclei and the other three outer rings and the central ring benzene nuclei.

According to Pavolini (222), lignin is a tetramer of special aromatic hydroxyaldehydes, as indicated below (formula XVII):



This formula is not in harmony with several experimental facts, particularly with the results obtained on heating lignin with hydriodic acid, and with those obtained on the distillation of lignin with zinc dust in an atmosphere of hydrogen.

An hypothetical structural formula (XVIII) for lignin, which is intended to account for several facts concerning its chemistry, has also been proposed by Fuchs (81).



XVIII

XIX. METABOLISM

Although many of the materials of plant origin that are used as food by man and animals contain lignin in substantial amounts, it is rather surprising that such a common food ingredient has not been studied and subjected to metabolism experiments to a greater extent than that found recorded in the literature.

Several investigators, among them Meissner and Shepard (202), Harten (108), Weiske (297), and more recently König (177), have suggested that lignin probably furnishes the aromatic group involved in the formation of hippuric acid, but they have presented no experimental evidence in support of this claim. The last-named investigator, working with Dietrich (33) in 1871, as well as Stutzer (277), has claimed, however, that lignin is not digested in the animal body. König and Becker (178) found that the lignin of wheat bran was not digested by rabbits, whereas free lignin was digested by these animals to the extent of 12.8 per cent. According to Paloheimo (216), lignin reappears quantitatively in the feces. Rosgozinski and Starzewska (253) experimenting with sheep found that the lignin of oat straw and that prepared by Beckmann's method were not digested by

these animals. Rubner (256) noted a loss of lignin in experiments conducted with human beings as well as with dogs. Phillips, Weihe, Jones, and Csonka (238) and later Csonka, Phillips, and Jones (27) reported that lignin prepared from corn cobs by the alkali method, when fed to cows or dogs, caused an increase in the benzoic acid (hippuric acid) eliminated in the urine. In table 9 are presented some of the data obtained in their experiments in which a dog was used as the experimental animal.

TABLE 9

Lignin feeding experiments with dog showing effect on hippuric acid (benzoic acid) elimination

MEAT FED DAILY	LIGNIN ADDED TO MEAT DIET	TOTAL BENZOIC ACID ELIMINATED DAILY
<i>grams</i>	<i>grams</i>	<i>grams</i>
150	None	0.357
150	25	0.648
150	25	0.879
150	25	0.676
150	25	0.795
150	25	0.810
150	None	0.359
150	None	0.339
None	None	0.207
None	25	0.705

TABLE 10

Methoxyl group balance in metabolism experiments

EXPERIMENTAL ANIMAL	FORE PERIOD DAILY METHOXYL			EXPERIMENTAL PERIOD				
	Intake in food	Output in feces	Loss	Methoxyl in lignin added	Total methoxyl output in feces	Increase over normal output due to lignin	Loss of methoxyl in lignin added	
	<i>grams</i>	<i>grams</i>	<i>per cent</i>	<i>grams</i>	<i>grams</i>	<i>grams</i>	<i>grams</i>	<i>per cent</i>
Dog	None	None	—	13.0	10.4	10.4	2.6	20.0
Dog	None	None	—	13.48	11.67	11.67	1.81	13.3
Cow	249.5	77.8	68.8	210.80	522.20	133.30	77.50	36.7

In two lignin feeding experiments with cows the average daily output of benzoic acid increased from 32.34 to 45.08 and from 62.12 to 64.85 g. The total quantity of methoxyl in the lignin fed and in the feces was also determined, and the results showed a distinct loss of this group, as can be seen from table 10.

Results of digestion experiments conducted *in vitro* using the fresh

material from a cow's stomach and also the stomach juice indicated that demethoxylation of lignin had taken place. This apparently was not brought about by bacteria, but rather by some other agent, possibly an enzyme present in the gastric juice of the animal.

It may be concluded from the above that the results of the more recent lignin metabolism experiments indicate that this substance is, at least in part, broken down by the digestive processes of the animal body.

XX. MICROBIOLOGICAL DECOMPOSITION

There appears to be a decided difference, in so far as the action of fungi and bacteria are concerned, between lignin as it occurs naturally in plants and free or isolated lignin. Willstätter lignin or lignin isolated by the 72 per cent sulfuric acid method appears to be very resistant to the action of soil microorganisms and to the wood-destroying fungi *Trametes pini* and *Polystictus hirsutus* (262). Natural lignin under aerobic conditions can be decomposed by soil microorganisms, at least in part, although the rate of decomposition is generally less than that of the cellulose and hemicelluloses (239a).

According to Waksman and Gerretsen (292), the decomposition of the lignin of straw is affected considerably by temperature. At 7°C. the loss of lignin was negligible, whereas at 37°C. over 30 per cent of the lignin was removed in 3½ months and 50 to 60 per cent in 9 months.

Waksman and Nissen (294) found that the cultivated mushroom (*Agaricus campestris*) when grown on horse manure reduced the lignin content of this material from 20.8 per cent to 14.8 per cent in 47 days. The reduction of the lignin in the composted manure accounted for nearly 80 per cent of the total reduction in the weight of the original material.

Waksman and Tenney (239b and c) found that under anaerobic conditions the lignin of alfalfa was preserved practically quantitatively. Because of the relative resistance of the lignin of plant materials to microbial attack under certain natural soil conditions, Waksman and coworkers (291) have concluded that lignin contributes largely, though not exclusively, to the formation of humus. Fischer (45) has suggested that peat and coal originated largely from lignin. According to this theory, under the anaerobic conditions prevailing in peat bogs, the other plant constituents, such as cellulose and hemicellulose, are decomposed into gaseous and water-soluble products, whereas the lignin, being more resistant, accumulates. Subsequently, the methoxyl groups of the lignin are removed by hydrolysis, yielding humin-like bodies which enter into the formation of coal.

Rose and Lisse (254) made a chemical examination of a sound sample of Douglas fir heart and also of one partly rotted and of one almost completely rotted. They found that the percentage of cellulose and pentosans de-

creased with the advance in the decomposition of the wood, whereas the alkali-soluble fraction and the percentage of methoxyl increased. They concluded from their results that lignin is far more resistant to decomposition than cellulose, although no direct lignin determinations were made and no attempt was made to identify the fungi responsible for the decay. It has been known for some time that wood parasitic fungi, such as *Trametes pini*, *Polystictus hirsutus*, and *Polyporus annosus*, preferentially, though not exclusively, attack lignin, producing what is known as "white rot," whereas the organisms producing "brown rot" attack lignin only to a very limited extent (109).

Falck and Haag (43) conclude from their studies that in the microbiological decomposition of plant materials two distinct processes take place, namely, "destruction" and "corrosion." The effect of "destruction" is to decompose the cellulose and pentosans, the lignin being very little affected. "Corrosion," on the other hand, causes principally the decomposition of the lignin. "Destruction" may follow "corrosion," but not vice versa.

Studies of the microbiological decomposition of lignin or lignified materials have thus far afforded no degradation product that would help to throw light on the constitution of lignin. Pringsheim and Fuchs (244), after adding the necessary inorganic salts, inoculated alkali lignin with forest soil. The product obtained differed from the original material in containing up to one-half of its weight of substances soluble in alcohol, although the original lignin was practically insoluble in alcohol. The alcohol-soluble fraction was found to have a smaller percentage of methoxyl but a greater percentage of carbon than the original lignin. The fraction insoluble in alcohol showed some decrease in the percentage of methoxyl, but the percentage of carbon was not affected. No substance of a definite character was isolated.

Jensen (144) and also Waksman and Iyer (293) found that lignin has a depressing effect upon the decomposition of protein as measured by the evolution of carbon dioxide and the formation of ammonia. Alkali lignin (5 parts) was dissolved in sodium hydroxide solution, and 1 part of casein dissolved in the same solvent added. Acid was added until the pH was 7.0. The precipitate, designated as "humus nucleus" or "ligno-protein" complex, was found to be resistant to the action of microorganisms. The depressive effect on the decomposition of proteins by lignin was found to be due not to any toxic action of the lignin but to the fact that as a result of the interaction of the lignin and the protein a "ligno-protein" complex was formed which was resistant to microbial attack.

Many of the contradictory statements found in the literature on the microbiological decomposition of lignin and lignified materials can be

attributed to the fact that our present methods for the quantitative determination of lignin are faulty, and more definite and conclusive information must wait the development of more exact analytical methods.

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MOLECULAR DIFFUSION IN SOLUTION

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Diffusion is one of the most fundamental properties of substances in solution. If, for example, sugar is placed in a beaker of water and allowed to stand, the sugar will subsequently be found in all parts of the water. The same is true of other soluble substances, and we say that they diffuse throughout the water occupying the volume of the liquid just as any gas occupies the volume in which it is confined. The diffusion of molecules through liquids is a common phenomenon, and it has been extensively studied in a quantitative way. It should be remarked that in many cases the data of these experiments are conflicting and in other ways unsatisfactory, undoubtedly because each figure is usually the result of a prolonged and laborious experiment which is dependent upon the most painstaking precautions and observations.

These data have not always led to conclusions of theoretical importance because the kinetic theory of liquids is extremely difficult compared to that for gases and solids. However, for dilute solutions results of considerable significance can be obtained using the fundamental diffusion laws. In more concentrated solutions the elementary laws do not hold, supposedly because of interactions between dissolved particles and with solvent molecules which lead to association and solvation effects. Thus the situation may be compared to that of solutions of electrolytes, where the ideal limiting laws are known to be obeyed only in extremely dilute solutions and the deviations from them in more concentrated solutions are just beginning to be understood.

But within the limited scope suggested above, the writers feel that the diffusion theory has performed remarkably well in the interpretation of experimental data in a simple and straightforward way. It will be their attempt to treat these achievements in a logical way, discussing the *theory, experiment, interpretation, and application* of molecular diffusion in solution. At the same time it is desired to suggest the subject as one worthy and necessary of further investigation and development. It is our regret that in connection with many ideas expressed it will be impossible to give proper reference to excellent articles which, appearing from time to time, have embodied these thoughts.

Diffusion experiments achieved considerable importance in the hands of Graham (27) who used them to differentiate between "crystalloids" and "colloids." Both free diffusion and diffusion through membranes (dialysis) were used for this purpose. At least in the case of the free diffusion this separation depended upon a difference in the diffusion rate, and not on the fact that crystalloids diffuse and colloids do not. As this has become more clearly understood, it has become proper to speak of a "colloidal state of aggregation" rather than to think of "colloidal substances." As a matter of fact, both ordinary solutions and colloidal solutions are now recognized to be dispersed systems that comprise a dispersion medium and a dispersed part to which, among other things, the molecular kinetic theory may be applied. It is meant to imply here that the kinetic energy of suspended particles in a sol should be the same as the kinetic energy of molecules, and the colloidal solutions should give diffusion just as ordinary solutions do. We are thinking therefore in this article of molecular diffusion in its broader sense.

It is also well to mention that, unless noted to the contrary, a free diffusion is being considered. The mathematical theory of obstructed and forced diffusions is quite different from that of free diffusion. This point is emphasized because in several recent investigations the attempt has been made to avoid the experimental inconveniences of free diffusion by studying the rates of diffusion through porous membranes, giving a diffusion constant relative to some arbitrary standard. Diffusion constants obtained in this way hardly can be accepted as final when a demonstration of the sufficiency of the method is not provided.

I. THEORY¹

A. FREE DIFFUSION

In 1855 Fick (18) stated the general law of linear diffusion as follows: The quantity of substance which diffuses through a given area is proportional to the difference between the concentration of two areas infinitely near to each other. Expressed mathematically, if we take two points in a solution at a distance apart dx , with difference in concentration at these two points dc , concentration gradient in the direction x will be dc/dx and

¹ In the preparation of this section the authors have drawn freely from several sources, among which may be mentioned: Byerly, *Fourier Series and Spherical Harmonics*, Ginn and Co., New York (1893); Ingersoll and Zobel, *Mathematical Theory of Heat Conduction*, Ginn and Co., New York (1913); Carslaw, *Heat Conduction*, The MacMillan Co., New York (1921); Fürth, *Diffusion ohne Scheidewände*, *Handb. d. phys. u. techn. Mech.* (Auerbach-Hort), Vol. 7, Barth, Leipzig (1931).

the amount of solute, dm , which diffuses through a cross-section q in time dt is

$$dm = - Dq \frac{dc}{dx} dt \quad (1)$$

The minus sign means simply that the solute diffuses in the direction of decreasing concentration. This law, sometimes referred to as the first law of Fick, was originally empirical in character, but it has long since been shown to be derivable from osmotic theory. It is a typical "dilute solution" law. The constant D , the so-called diffusion constant or specific diffusion rate, measures the amount of solute which would diffuse across unit area under unit concentration gradient in unit time, provided the rate is constant during that time.

The two independent variables, x and t , and two dependent ones, m and c , make its use somewhat cumbersome. However, it is possible to reduce the number of dependent variables by one, obtaining at the same time the general differential equation of diffusion known as the second law of Fick. If we consider an infinitesimal volume in a space bounded by planes at the distances x and $x + dx$, the amount of solute which will accumulate in this volume in time dt will be the difference in the amount which enters across the plane at x and leaves across the plane at $x + dx$. It will be

$$dm - (dm + \frac{\partial(dm)}{\partial x} dx) = - \frac{\partial(dm)}{\partial x} dx$$

Now, since concentration is amount divided by volume, the corresponding concentration increase is

$$- \frac{\frac{\partial(dm)}{\partial x} dx}{q dx}$$

This concentration increase is also expressed by the quantity $\frac{\partial c}{\partial t} dt$, therefore

$$\frac{\partial c}{\partial t} dt = \frac{1}{q} \frac{\partial(dm)}{\partial x}$$

Combination of this expression with the first law of Fick leads directly to the very important and general result

$$\frac{\partial c}{\partial t} = D \frac{\partial^2 c}{\partial x^2} \quad (2)$$

The diffusion law may also be derived hydrodynamically. If the solu-

tion to which it is applied is sufficiently dilute for the use of the ideal gas law to measure its osmotic pressure we have,

$$p = C \frac{RT}{M}$$

where C is the concentration (amount per unit volume) and M is the molecular weight of the solute. Now, if we consider a volume element, dV , the force on the dissolved particles due to differences in p will be

$$F = - \text{grad } p \, dV$$

But if m is the mass of a single particle, the total number of particles in dV is $\frac{C}{m} dV$, so that the force on a single particle will be

$$f = - \frac{m}{C} \text{grad } p$$

Now, since $M/m = N$, we can write

$$f = - \frac{RT}{N} \frac{\text{grad } C}{C}$$

For the case of steady motion, that is, where each particle is given a constant velocity v , it is evident that

$$v = Bf$$

where B is the "mobility" of the particle. It depends upon the size and shape of the particle and the viscosity of the medium in which it is suspended. Therefore,

$$v = - \frac{RT}{N} B \frac{\text{grad } C}{C}$$

Expressed in terms of the flow, J , which is by definition the product $C \cdot v$, we have,

$$J = C \cdot v = - \frac{RT}{N} B \text{grad } C = - D \text{grad } C \quad (3)$$

The diffusion equation is sometimes used in this simple and direct form, a good example of its application being found in the recent work of Onsager and Fuoss (66). The identity $D = RT/N \cdot B$ will be established in a later section.

The diffusion law has different solutions according to the conditions imposed by the methods of carrying out the experiment. This may be illustrated best perhaps by working out the most general solution in the infinite first, and then showing how it is applied to specific problems. In

another section there are considered the modifications necessary when the diffusion takes place in such a way that the process is limited by the presence of a boundary.

I. Solutions without finite boundary

The conditions which must be met by any physical solution are as follows:

1. $c = c(x, t)$.
2. When $t = 0$, $c = f(x)$.
3. When $t > 0$, $f(x)$ can be differentiated.

The general solution is obtained by assuming

$$C = \Phi(x)\Psi(t) \quad (4)$$

This makes it possible to separate the variables in equation 2, giving two ordinary differential equations whose solutions are

$$\begin{aligned} \Phi(x) &= \beta \cos kx + \gamma \sin kx \\ \Psi(t) &= \alpha \cdot e^{-k^2Dt} \end{aligned} \quad (5)$$

in which α , β , γ , and k are real constants. Since any sum of solutions is also a solution, a new solution results if we add solutions of the form 5 and integrate over all positive values of k . The constants β and γ are taken as functions of k . The result of the operation is

$$C = \int_0^\infty (g(k) \cos kx + h(k) \sin kx) e^{-k^2Dt} dk \quad (6)$$

in which $g(k)$ and $h(k)$ are arbitrary functions of k . The problem now is to see whether these functions can be so chosen that the second condition above is fulfilled, that is, we can write

$$f(x) = \int_0^\infty (g(k) \cos kx + h(k) \sin kx) dk \quad (7)$$

Fourier has found this to be the case when the functions $g(k)$ and $h(k)$ are chosen in the following manner:

$$\begin{aligned} g(k) &= \frac{1}{\pi} \int_{-\infty}^{+\infty} f(\alpha) \cos \alpha k d\alpha \\ h(k) &= \frac{1}{\pi} \int_{-\infty}^{+\infty} f(\alpha) \sin \alpha k d\alpha \end{aligned}$$

Substitution of these values in equation 6 leads to the result

$$C = \frac{1}{\pi} \int_0^{\infty} e^{-k^2 D t} dk \int_{-\infty}^{+\infty} f(\alpha) \cos k(\alpha - x) d\alpha \quad (8)$$

Thus, it can be shown by an integration process that the general solution of Fick's second law for diffusion in the x direction is

$$C = \frac{1}{2\sqrt{\pi D t}} \int_{-\infty}^{+\infty} f(\alpha) e^{-\frac{(\alpha - x)^2}{4 D t}} d\alpha \quad (9)$$

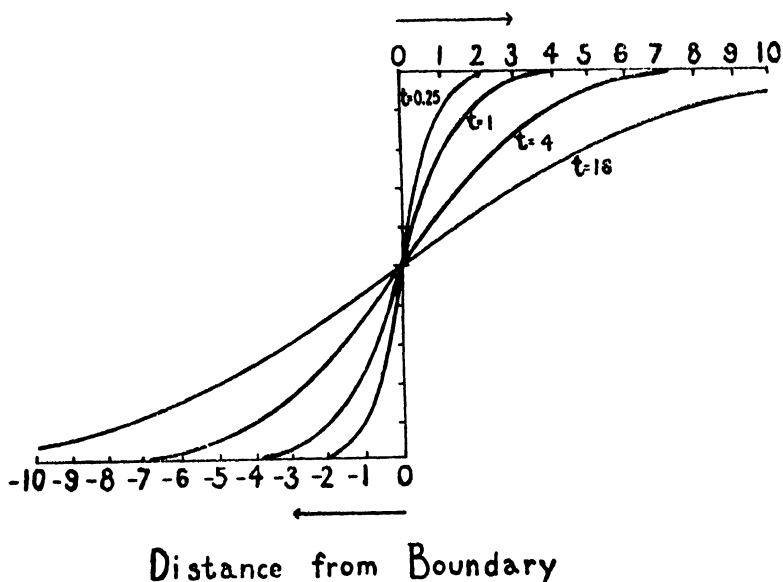


FIG. 1. RELATIVE CONCENTRATION AS A FUNCTION OF DISTANCE FROM BOUNDARY.
DIFFUSION FROM SOLUTION ACROSS BOUNDARY INTO SOLVENT

By the introduction of the new variable

$$y = \frac{\alpha - x}{2\sqrt{Dt}}$$

the general solution becomes

$$C = \frac{1}{\sqrt{\pi}} \int_{-\infty}^{+\infty} f(x + 2y\sqrt{Dt}) e^{-y^2} dy \quad (10)$$

The brief description of two very important special cases of the application of this equation to the diffusion of solutes will illustrate its use. It may be well to recall that in these cases the diffusion is not restricted by

the dimensions of the cell in which the process is taking place; in other words, the containing vessels are long enough and the time is short enough so that the concentration changes do not occur at their extreme ends.

Case I. Diffusion from solution into solvent. At time $t = 0$ the concentration of the solute in the positive half of the cell is C_0 , but in the negative half it is zero. Thus

$$f(\alpha) = 0, \text{ for } \alpha < 0$$

$$f(\alpha) = C_0, \text{ for } \alpha > 0$$

Under these conditions

$$C = \frac{C_0}{2} \left\{ 1 - U \left(\frac{x}{2\sqrt{Dt}} \right) \right\} \quad (11)$$

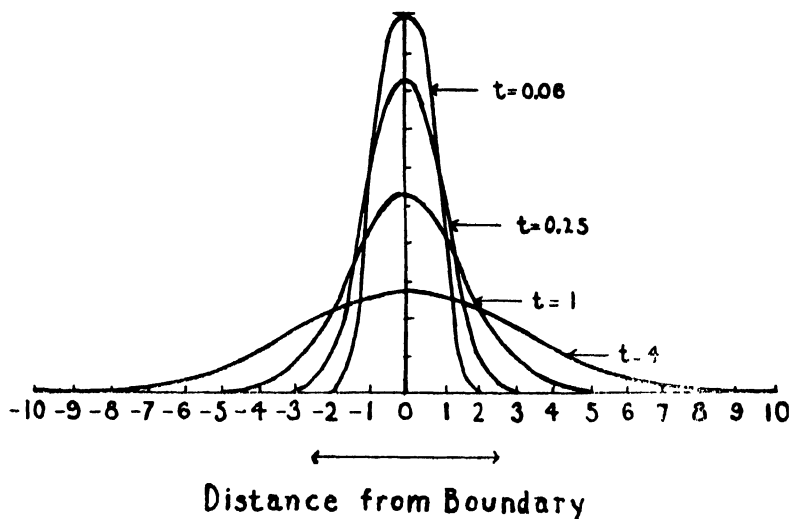


FIG. 2. RELATIVE CONCENTRATION AS A FUNCTION OF DISTANCE FROM BOUNDARY. DIFFUSION FROM THIN LAYER INTO SOLVENT

where

$$U(x) = \frac{2}{\sqrt{\pi}} \int_0^x e^{-y^2} dy$$

The progress of such a diffusion as a function of distance for definite times is shown by the accompanying graph (figure 1) obtained from equation 11.

Case II. Diffusion from thin layer. At time $t = 0$ the concentration of the solute in the cylinder is zero except for an infinitely thin layer of thick-

ness dx between the positive and negative halves of the vessel, in which it becomes infinite as the thickness approaches zero. Thus,

$$f(\alpha) = 0, \text{ for } \alpha > 0$$

$$f(\alpha) d\alpha = 1, \text{ for } \alpha = 0$$

Under these conditions

$$C = \frac{1}{2\sqrt{\pi Dt}} e^{-\frac{x^2}{4Dt}} \quad (12)$$

Figure 2 shows the progress of this type of diffusion. Here $C(x)$ is shown at a number of times t .

II. Solutions with finite boundary

In the general solution of the linear problem it was assumed that the medium in which the diffusion took place extended to infinity in both positive and negative directions. It is not difficult to extend this solution to certain cases where the medium extends to infinity in the one direction but is bounded by a surface on the other side. This surface is conveniently chosen at position $x = 0$. In such an experiment with smooth and impervious boundary at right angles to the direction of the diffusion, $\partial c/\partial x = 0$ for $x = 0$, and the general solution of Fick's law assumes the form

$$C = \frac{1}{2\sqrt{\pi Dt}} \int_0^\infty f(\alpha) \left\{ e^{-\frac{(\alpha-x)^2}{4Dt}} + e^{-\frac{(\alpha+x)^2}{4Dt}} \right\} d\alpha \quad (13)$$

Corresponding to the second special case considered above, let us assume an experiment in which there is a very thin layer of diffusing solution under a very high column of dispersion medium. As before

$$f(\alpha) = 0, \text{ for } \alpha > 0$$

$$f(\alpha) d\alpha = 1, \text{ for } \alpha = 0$$

and

$$C = \frac{1}{\sqrt{\pi Dt}} e^{-\frac{x^2}{4Dt}} \quad (14)$$

As might have been predicted, the concentration at any distance x in time t is twice that obtained before.

Another important finite boundary problem is the diffusion between parallel boundaries in the YZ planes, $x = 0$ and $x = l$. At time $t = 0$, $c = f(x)$ and $0 \leq x \leq l$. It has already been shown that the expression

$$e^{-k^2 Dt} (A \cos kx + B \sin kx)$$

is a solution of the general diffusion law when A , B , and k are chosen properly. The boundary conditions of the problem demand that $A = 0$ and $kl = n\pi$, where $n = 1, 2, 3, \dots$ etc. The particular solution then becomes

$$B_n \sin \frac{n\pi}{l} x \cdot e^{-\frac{n^2\pi^2}{l^2} Dt}$$

Any sum of linear solutions is also a solution, therefore

$$C = \sum_{n=1}^{\infty} B_n \sin \frac{n\pi}{l} x \cdot e^{-\frac{n^2\pi^2}{l^2} Dt}$$

Such an infinite sum is a solution provided the series converges. The coefficients B_n may be obtained from conditions at the start of the experiment. It is required that

$$f(x) = \sum_{n=1}^{\infty} B_n \sin \frac{n\pi}{l} \cdot x \text{ in the region } 0 \leq x \leq l$$

Fourier has shown that this is fulfilled since $f(x)$ can be represented by a series of sines, cosines or both, and the coefficients are

$$B_n = \frac{2}{l} \int_0^l f(\alpha) \sin \frac{n\pi}{l} \alpha \, d\alpha$$

Thus

$$C = \frac{2}{l} \sum_{n=1}^{\infty} e^{-\left(\frac{n\pi}{l}\right)^2 Dt} \sin \frac{n\pi}{l} x \cdot \int_0^l f(\alpha) \sin \frac{n\pi}{l} \alpha \, d\alpha \quad (15)$$

This equation is an extremely important one because it is required for the calculation of the diffusion constant in several types of experiment.

An important diffusion experiment makes use of conditions described by Stefan (79), as follows:

At time $t = 0$ the space between planes $x = 0$ and $x = h$ is filled with solution of concentration $C = C_0$ and the corresponding space between $x = h$ and $x = l$ is occupied by solvent, and $c = 0$. In this event,

$$f(x) = C_0, \text{ for } 0 \leq x < h$$

$$f(x) = 0, \text{ for } h < x \leq l$$

Transformations not detailed here lead to the final result

$$C = C_0 \left(\frac{h}{l} + \frac{2}{\pi} \sum_{n=1}^{\infty} \frac{1}{n} e^{-\left(\frac{n\pi}{l}\right)^2 Dt} \cos \frac{n\pi}{l} x \cdot \sin \frac{n\pi}{l} h \right) \quad (16)$$

The use of this rather complicated formula may be simplified by choosing the experimental conditions in such a way that the ratio h/l is some simple fraction. Its use is also rendered less tedious by the tables of Stefan (79) and Kawalki (40), which are constructed for the case where $h = l/4$. If we know the amount of substance in the several layers into which the diffusing liquid can be divided, the diffusion constant D can be calculated.

In certain experiments it is important to know how much material has diffused from one layer into another in a given time. Thus, for the case in which $h = l/2$, the quantity Q , which has penetrated into the solvent, is

$$Q = - \int_0^t D \left(\frac{\partial c}{\partial x} \right)_{x=\frac{l}{2}} dt$$

$$= \frac{lc_0}{4} \left\{ 1 - \frac{8}{\pi^2} \sum_{m=0}^{\infty} \frac{1}{(2m+1)^2} e^{-\left[\frac{(2m+1)\pi}{l} \right]^2 Dt} \right\} \quad (17)$$

An additional type of experiment in which material is allowed to diffuse into a porous solid or gel from a stirred liquid in contact with it is of considerable chemical interest, but unfortunately the classical methods of Fourier analysis do not always provide adequate solution of the mathematical problem, and other treatments have been necessary. It is largely through the efforts of March and Weaver (49) and of Langer (47) that the coefficients of the several terms can now be determined, with the result that the specific diffusion rate into the porous solid or gel may be calculated from the analysis of the concentration of the stirred liquid above it as a function of the time.

The question may properly be raised at this point whether a free or obstructed diffusion will take place under these conditions. Its answer will depend primarily upon the relative size of the pore and diffusing molecule, because it will determine whether or not the neighborhood of the extensive surfaces within the structure of the solid affects the nature or extent of the diffusion. There may be a suppression of the diffusion through the orientation and immobilization of solvent molecules adjacent to these surfaces; there may be mechanical blocking; there may be orientation effects if the diffusing molecules differ from the spherical shape to any considerable degree—these and other factors would cause an obstructed diffusion where the pore diameters are not very much larger than those of the diffusing molecules. We shall see that experiments which permit the comparison of the obstructed and free diffusion rates may lead to valuable information with regard to the structure of the diaphragm.

In the March and Weaver treatment of the problem there is assumed a mass of a material to be uniformly distributed, at time zero, in such a solid

of given depth. The solid is then covered with water to the same depth. The water is kept stirred during the experiment in which the material diffuses into the water. For the mathematical treatment there is obtained a Volterra integral equation of the second kind with discontinuous kernel to express the concentration in the liquid as a function of the time. The solution of this integral equation is obtained in terms of the roots of a transcendental equation and the roots of an infinite system of linear equations. By means of the theory of singular integral equations, it is shown that the differential equation and boundary conditions possess but one solution of the required type. This solution is

$$V = \frac{U + \lambda V_0}{1 + \lambda} - \sum \frac{B_i}{\beta_i} e^{-\beta_i t} \quad (18)$$

where V is the fraction of the material which has diffused from the solid,
 λ is the ratio of the height of the solid to the height of the liquid
 above it, in this case unity,

t is the time,

$U + \lambda V_0 = 1$, and represents the sum of the solute in the solid
 and water above,

and the quantities B_i and β_i are more complicated functions which depend upon the boundary conditions, the time, and the diffusion constant.

Complete details for the determination of these coefficients are given in the original article. After their evaluation the expression for the concentration in the liquid becomes

$$V = \frac{1}{2} - [0.327 e^{-4.117T} + 0.0766 e^{-24.14T} + 0.0306 e^{-63.68T} + 0.0160 e^{-123T} + \dots]$$

where $T = Dt/a^2$, D is the diffusion constant, t is the time, and a is the height of the solid or of the liquid column above it. The diffusion constant is obtained most readily by plotting V as a function of T , according to this equation. The quantity V is the one determined experimentally as the time proceeds. For each value of V there is found on the graph the corresponding value of T , and since both a and t are known, the value of the diffusion constant is thereby fixed.

B. FORCED DIFFUSION

If there acts on a dissolved particle an external force f^* , causing an additional velocity v^* , then the additional flow is $cv^* = cBf^*$ and the diffusion law assumes the form

$$\frac{\partial c}{\partial t} = D \frac{\partial^2 c}{\partial x^2} - v^* \frac{\partial c}{\partial x} = D \frac{\partial^2 c}{\partial x^2} - Bf^* \frac{\partial c}{\partial x} \quad (19)$$

The statistical equilibrium or the distribution of concentration in the solution which is independent of the time is found by solving the equation

$$D \frac{\partial^2 c}{\partial x^2} - v^* \frac{\partial c}{\partial x} = 0 \quad (19a)$$

In its general form the solution is

$$c = ae^{\frac{v^*}{D}x} + b \quad (20)$$

in which a and b are arbitrary constants. In many cases the boundary conditions require that $b = 0$. Thus for sedimentation equilibrium the solution takes the form of the well-known hyposometric law:

$$c = c_0 e^{-\frac{N}{RT} f^* x} = c_0 e^{-\frac{Mg}{RT} x} \quad (20a)$$

In this equation g is the acceleration due to gravity. Particular solutions of the general equation (19) have been obtained for a number of purposes. To mention a single example, they have considerable use in sedimentation studies with colloidal solutions in which the additional forces are either gravitational or centrifugal in character.

Another extremely important case of a diffusion under the influence of an external force is found in the process taking place in a solution containing electrolytes. Onsager and Fuoss (66), in a very complete treatment of the problem, have shown that fundamentally the diffusion and conduction belong together, both being problems involving the general migration of ions. They have concerned themselves with the formulation of the general differential equations directly in terms of the "driving forces" or gradients of thermodynamic potentials, rather than in terms of osmotic pressures which are related to thermodynamic potentials. In the case of an electrolyte containing two kinds of ions where the assumption of complete ionization can be made, Nernst (57) in 1888 derived an expression for the diffusion constant based upon values of the ionic mobilities as determined by conductance and transference number measurements at high dilution. This expression has been generalized by Noyes (30) to give the following result:

$$D = RT \cdot \frac{U_c \cdot U_a}{U_c + U_a} \left(\frac{1}{Z_c} + \frac{1}{Z_a} \right) \quad (21)$$

where U_c and U_a are the mobilities of the cation and anion, and Z_c and Z_a are their valences. This is a typical infinitely dilute solution law. In the region of finite, but very dilute, solutions (Debye-Hückel region), deviations from a random arrangement affect the resistance to the motion

of the ions. A dissociation into ions which is practically complete is assumed.

In the conductance problem the mobility directly due to the applied electrical field overcoming the ordinary friction of the solvent is modified, owing to these deviations from a random arrangement by two forces, the electrical force of relaxation and the electrophoretic force. The diffusion of a simple electrolyte will be modified by the second of these forces only, since all the ions now migrate with the same velocity and no asymmetry can be developed in the ion atmospheres about them. The electrophoretic force, on the other hand, is dependent upon a volume force acting in the ionic atmosphere, resulting in an alteration of the forces needed to make both ions move with the same velocity. In a pure diffusion any velocity difference will be eliminated because of space charge effects. Onsager and Fuoss have shown that the electrophoretic effect may be divided into first and second order terms, both due to the deviations of the ions from a random arrangement. The first order effect results because the anions in the neighborhood of a given anion are partially replaced by cations, and vice versa. When one species of ions is more mobile than the other the slower ions will move in a countercurrent and the more mobile ions will be aided by a motion of their environment. This is a typical "square root of the concentration" effect. The second term, which always decreases the resistance to diffusion, depends upon an overall reduction of the mean distances between the ions in the sense that the distances between ions of opposite sign are reduced more than the distances between like ions are increased.

In more concentrated solutions the specific properties of electrolytes make the theoretical study a difficult one. If the amount of solvent is still large in comparison with that of the solute, the resistance offered by the medium will be practically independent of the concentration, but otherwise not. Haskell (30) has treated the situation which exists when both ions and undissociated molecules are present, by assuming that the frictional resistance encountered by an ion is different from that of the undissociated molecules, while the osmotic effects of ions and molecules are determined solely by their number, and has attempted to measure the difference in diffusion rate existing between the dissociated and undissociated portions of the solute. In general, ions are believed to move more rapidly than molecules because the diffusion rate usually increases with dilution. The equation set up is

$$\frac{\partial c}{\partial t} = D_1 \frac{\partial^2 c_1}{\partial x^2} + D_2 \frac{\partial^2 c_2}{\partial x^2} \quad (22)$$

where the subscripts 1 and 2 refer to neutral molecules and ions, respectively. The equation could be simplified so as to contain only one independent variable c_2 , but it had to be used in differential form. Equations containing only D_1 and D_2 were set up by assuming the concentration c_2 to be proportional to the specific conductance and the degree of dissociation to be measured by the classical Arrhenius conductance ratio. The best values of D_1 and D_2 were obtained from these equations using the method of least squares. The values of D_2 obtained agree very well indeed with values calculated using the Nernst equation, and are claimed to confirm the assumptions involved in the calculations, but in the light of more recent theoretical developments it seems well to reserve judgment until further experimental work can be done.

DIFFUSION AND BROWNIAN MOVEMENT

We owe the theory of the Brownian movement from the molecular kinetic point of view to Einstein (17) and to Smoluchowski (76). The displacement of the molecule or particle during a certain interval of time characterizes the movement. Considering linear motion along one direction (x) only, it is evident that positive and negative displacements are equally probable; furthermore the smaller displacements are more probable than the larger ones. The probability of a horizontal displacement having a value between x and $x + dx$ is

$$P = \frac{1}{\sqrt{2\pi\Delta_l^2}} e^{-\frac{x^2}{2\Delta_l^2}} dx \quad (23)$$

where Δ_l^2 is the mean of the square of the average displacement in a linear direction.

It now turns out that the mean displacement Δ_l is quite simply related to the diffusion constant, a result of tremendous significance. The argument of Einstein is as follows: Suppose the diffusion to take place across a plane in a horizontal tube, with concentrations c_1 and c_2 to the left and right of this plane, respectively. In the time t only those particles closer to the plane than the mean displacement Δ_l can pass through it, and their number will be $1/2 \Delta_l(c_1 - c_2)$. If Δ_l is small,

$$\frac{c_2 - c_1}{\Delta_l} = \frac{dc}{dx}$$

Therefore the number of molecules passing the plane in unit time is

$$- \frac{1}{2} \frac{\Delta_l^2}{t} \frac{dc}{dx}$$

But, by Fick's first law, the coefficient of diffusion D is the number of molecules passing unit cross-section in unit time when the concentration gradient $-dc/dx = 1$. Therefore,

$$D = \frac{1}{2} \frac{\Delta_l^2}{t} \quad (24)$$

and

$$P = \frac{1}{2\sqrt{\pi Dt}} e^{-\frac{x^2}{4Dt}} dx \quad (25)$$

which, as we have seen, is a solution of Fick's second law.

Einstein has also shown the coefficient of diffusion to be related to the size of the molecules and the viscosity of the liquid. If the velocity of a diffusing molecule is v

$$v = Bf$$

where f is the force exerted on the molecule and B is its "mobility" or the reciprocal of the frictional resistance experienced by it. If the concentration of the solution before the plane is c , there will be cN molecules involved, with force F acting upon them, and

$$v = \frac{1}{cN} FB$$

In the diffusion the force acting is the osmotic pressure gradient, therefore

$$F = - \frac{dP}{dx} = - RT \frac{dc}{dx}$$

and

$$vc = - \frac{RT}{N} B \frac{dc}{dx} \quad (26)$$

Again making use of the first law of Fick it is evident that

$$D = \frac{RT}{N} B \quad (27)$$

If the molecule can be assumed to be spherical, the frictional resistance may be expressed in terms of its radius, r , and the coefficient of friction of the medium, η , by means of Stokes' law, provided certain other requirements are met, with the final result.

$$D = \frac{RT}{N} \cdot \frac{1}{6\pi\eta r} \quad (28)$$

This equation is known in the literature as the Stokes-Einstein law.

ROTARY DIFFUSION CONSTANT

In addition to the Brownian movement of translation, molecules and particles are undergoing rotational motion, owing to an unequal distribution of molecular impacts upon the faces of the parts of the particle on each side of the axes of rotation, and it follows from kinetic theory that the mean energy of rotation will be equal to the mean energy of translation. It has been shown a number of times that the x of the deduction of the previous section may be replaced by another coördinate a , the angle of rotation, since a itself is not contained in the expression for the kinetic energy, and its derivative with respect to time, da/dt , appears only in terms with constant coefficients. Thus a formula which looks just like equation 24 is obtained, that is,

$$D_r = \frac{1}{2} \frac{\Delta_r^2}{t}$$

where D_r is the rotary diffusion constant, and Δ_r^2 is the mean of the square of the average displacement in a rotary motion.

In the case of the rotational motion, another law of Stokes becomes applicable provided the molecule can be considered to be a sphere. This law says that if a torque of moment I be applied to a sphere of radius r in a medium of viscosity η , the angular velocity acquired by the sphere will be $\frac{I}{8\pi\eta r^3}$. Thus, the mobility of the system, B , referred to the angular motion will be

$$B = \frac{1}{8\pi\eta r^3} \quad (29)$$

and the rotary diffusion constant becomes

$$D_r = \frac{RT}{N} \cdot \frac{1}{8\pi\eta r^3} \quad (30)$$

The experimental determination of D_r is a matter of considerable difficulty. It is true that Perrin (67) was able to make a direct microscopic observation of the mean rotation of particles, using mastic globules having a radius of 6.5×10^{-4} cm. and with small enclosures of impurities on the surface of these globules to enable him to observe the rotary motion, but in general it will not be possible to test the fundamental equations for the motion in this way. Very recently, however, theoretical developments have made available two types of experiment whereby this desired result may be realized, and it seems worth while to outline them. The first development is due to Boeder (6) and depends upon the fact that the

optical birefringence induced by flow in solutions arises from the tendency of nonspherical particles to orient, owing to the mechanical stresses within the fluid. This theory should be extended to the double refraction produced by a magnetic field, because it seems possible under these conditions to obtain a higher degree of precision. The second method for the determination of a rotary diffusion constant is based upon the dipole theory of Debye (14). As far as we are aware it has not been specifically mentioned in this connection, although several investigators have proposed to use the dipole theory as a method for the determination of particle size.

The principles upon which the theoretical work of Boeder is based may be given by three statements.

1. The mechanical flow of the solution containing nonspherical molecules or particles causes an orientation of these odd-shaped units.

2. This orientative tendency is opposed by their Brownian movement, the disarranging tendency of which is characterized by the diffusion constant, D_r .

3. If the character of the stresses arising from the viscous flow is known, and if the resulting equilibrium state between the two tendencies can be determined (measurement of double refraction), the diffusion constant can be found.

To these statements a fourth and more obvious one, specifically mentioned by Kuhn (44), may be added:

4. Knowing the diffusion constant, information about the size and also the shape of the molecule or particle should result.

Thus, the problem is one of a rotary diffusion influenced by an external force, in this case produced by the rotation of the inner cylinder of a Stormer type of viscometer. The effect of this rotation upon a particle with direction ϕ is to give it an angular velocity

$$\omega(\phi) = -\beta \sin^2\phi \quad (31)$$

where β is the radial velocity gradient of the fluid motion, and ω is the induced angular velocity of the long axis of the particle.

The directional distribution of the particles is governed by the law of Fick,

$$\frac{\partial \rho}{\partial t} = D_r \left(\frac{\partial^2 \rho}{\partial \phi^2} \right) \quad (32)$$

where ρ is the number of particles whose long axes lie in the interval ϕ and $\phi + d\phi$, or the direction density. The combined effect of these forces is given by the relation

$$\frac{\partial \rho}{\partial t} = D_r \left(\frac{\partial^2 \rho}{\partial \phi^2} \right) - \frac{\partial(\rho\omega)}{\partial \phi} \quad (33)$$

At equilibrium $\partial\rho/\partial t = 0$, therefore

$$D_r \left(\frac{\partial^2 \rho}{\partial \phi^2} \right) - \frac{\partial(\rho\omega)}{\partial \phi} = 0 \quad (33a)$$

The solution of this equation, which we will not reproduce, gives the direction density ρ as a function of the direction angle ϕ , the radial velocity gradient of fluid motion β , and the diffusion constant, D_r . The aim to find D_r can be accomplished because means have been provided in the double refraction produced by the molecule or particle orientation to determine the state of equilibrium produced by a given constant rotation of the cylinder.

The second method for the determination of D_r depends upon the frequency dependence of the dielectric constant for a system composed of electrically dissymmetrical molecules suspended in a non-polar solvent medium. In such cases the dipole theory tells us there will be found to be a region in which the dielectric constant decreases as the frequency is increased, because a finite time is required for the orientation of the molecules in the electrical field, owing to the frictional resistance of the medium to the rotation.

The quantitative argument may be suggested by saying that at sufficiently high frequencies the dielectric constant will fall off because the inner friction constant of the medium prevents the orientation of the dipole molecules. The polarization of the system resulting from the suspended molecules consists of two parts, a polarization due to their deformation and a polarization due to their orientation, both of which contribute to the dielectric constant. The transition from the high dielectric constant, ϵ_0 , to the low dielectric constant, ϵ_∞ , will occur in a frequency region defined approximately by the equation,

$$\nu_c \tau = 1$$

where τ , called the time of relaxation of the molecules, is the time required for $1/e^{\text{th}}$ of the particles to assume a random distribution in the solution after the applied field has been removed, and ν_c is the critical frequency of the alternating field. This means simply that the anomalous dispersion occurs when ν_c and $1/\tau$ are of the same order of magnitude.

Actually the transition between the high and low values of the dielectric constant will take place in the frequency region defined by the expression,

$$0.1 \leq \chi \leq 10 \quad (34)$$

In this equation

$$\chi = \frac{\epsilon_0 + 2\pi\zeta\nu}{\epsilon_\infty + 2kT}$$

where ζ is the "inner-frictional" constant, which because of its existence makes necessary the exertion of a torque to rotate the molecules in the solution,

ν is the electrical frequency in cycles per second,

k is the Boltzmann constant, and

T is the absolute temperature.

The theory tells us that the observed dielectric constant will assume a mean value (that is, the dielectric constant-frequency curve will pass through a point of inflection) at the point where $\chi = 1$. Under these conditions,

$$\frac{\epsilon_0 + 2}{\epsilon_\infty + 2} \cdot \frac{\pi \zeta \nu_c}{kT} = 1 \quad (35)$$

with the result that

$$\nu_c \tau = \frac{\epsilon_\infty + 2}{\epsilon_0 + 2} \cdot \frac{1}{2\pi} \quad (36)$$

In order to obtain this result the quantity ζ has been replaced by its equivalent $\tau \cdot 2kT$. This equality is a consequence of the dipole theory which we cannot discuss here.

We have seen that when a sphere of radius r rotates in a liquid of viscosity η the frictional torque is $8\pi\eta r^3$ times the angular velocity of the sphere. Therefore, for such a sphere,

$$\zeta = 8\pi\eta r^3 \quad (37)$$

This application of the law of Stokes enables us to express the time of relaxation or critical frequency in terms of either the radius of the molecule or the diffusion constant, since

$$\tau = \frac{4\pi\eta r^3}{kT} = \frac{\epsilon_\infty + 2}{\epsilon_0 + 2} \cdot \frac{1}{2\pi\nu_c} \quad (38)$$

and

$$D_r = \frac{RT}{N} \cdot \frac{1}{8\pi\eta r^3} \quad (39)$$

The determination of the time of relaxation depends upon the experimental observation of ϵ_c , ϵ_∞ , and ν_c .

The problem which had to be solved in working out the theory of the anomalous dispersion was how to find the distribution function of the electric moments of molecules affected by a field variable with time. The general mathematical basis for the solution of this problem was found in

the theory of the Brownian movement as developed by Einstein (17). The number of molecules whose moments entered in the direction of a given solid angle during an interval of time δt was determined by two causes, one due to the applied alternating field, the other due to the rotary Brownian movement, and the effect of each had to be calculated.

Problems of the type discussed in this article, both as regards linear and rotational displacements, become much more difficult when the shape of the molecule or particle involved deviates from that of a sphere. Some progress has been made in extending the necessary calculations to ellipsoidal and rod-shaped particles, particularly in connection with viscosity problems. Therefore it can be expected that the necessary modifications of the theoretical work described above will be made in the near future, so that the results may be applied to molecules deviating from the spherical or nearly spherical shape. This is particularly necessary in the cases where optical effects produced in solutions are used to study the distribution of the molecules. It is of interest to remark that only very recently the importance of taking the diffusion and Brownian movements into account has been recognized. In a sense these are all problems of a diffusion influenced by an external force, and the effect of the diffusion can be neglected only when it can be shown to be negligible in comparison with the effects produced by the other forces involved.

II. EXPERIMENT

A very large number of methods have been worked out for the experimental study of diffusion. Since there is involved the relationship of three variables—concentration, distance, and time—the variations in method are largely reflected in the different ways chosen to measure these variables. The methods also differ in the way in which the boundary conditions postulated in the mathematical formulation are met. It cannot be too strongly emphasized that the mathematical development determines, and hence must precede, the establishment of experimental conditions and the design of the apparatus to be used.

There are several obvious conditions which should be met by any experimental method, as follows:

1. Change in concentration during an experiment should be small.
2. There should be no decomposition, association, or chemical reaction of the components of the system.
3. The diffusion constant must be independent of the concentration of the diffusing material, if Fick's law is to be used.
4. There must be a sharp initial interface.
5. There must be avoided any disturbance or temperature gradient which would cause streaming or mixing.

6. There must be no volume change during the experiment.
7. There must be available methods for accurate concentration determinations.

There exist in the literature several classifications of diffusion experiments. Of these, the methods of Cohen and Bruins (11) and of Fürth (24) have much to recommend them. However, we shall prefer to adopt a double classification, dividing the experiments, first, on the basis of the kind of observation made (measurement of concentration), and second, with respect to the type of diffusion experiment used. The tabulation based upon the kind of observation made to measure the concentration is independent of the way in which the experiment is set up to meet the boundary conditions postulated in the mathematical formulation. Practically all of the methods used to measure the concentration are applicable to either the continuous or interrupted type of experiment.

TABLE 1

Concentration measurement in diffusion experiments

1. Analytical	3. Optical
a. Gravimetric	a. Particle count
b. Volumetric	b. Refractive index
c. Colorimetric	c. Light absorption
d. Density	d. Wave length
2. Electrical	e. Optical rotation
a. Potential difference	f. Fluorescence
b. Resistance	

The several kinds of observations made to measure concentration are suggested by table 1. They involve both physical and chemical methods of measurement.

The analytical methods, because of their availability and application to the simpler types of diffusion apparatus, were commonly used by the earlier investigators. The determination of concentration by chemical analysis is usually made at the conclusion of the experiment on samples from different parts of the diffusion system. The course of the diffusion may be followed by chemical analyses only when the removal of the sample will not disturb the diffusion or cause an appreciable change of concentration in the cell. Colorimetric determinations include solutions obtained by the use of indicators and turbid solutions as well as those which follow Beer's law. Both the hydrometer and balance have been used for density determinations.

The electrical methods are restricted to systems whose components carry electrical charges. They are readily adapted to the making of con-

tinuous observations, but a small error in the electromotive force measurement represents a significant deviation in the concentration. The potentials are not always readily reproducible at low concentrations; in fact, accurate measurements of density, chemical composition, and potential difference all require rather concentrated solutions.

The optical methods are accurate, may usually be applied without disturbing the diffusing system, and may be used with organic substances. Further, dilute solutions may be used and only small amounts of material are required. The methods depending upon refractive index change are applicable only to those substances which do not absorb light.

Having suggested the means by which concentration may be measured, we are now ready to classify the systems as to type of apparatus used. It is convenient to describe them as:

A. Experiments in which the prevailing average concentration in

TABLE 2

General types of diffusion apparatus

A. Observation of finite layers at the conclusion of the experiment.	B. Continuous or intermittent observation of an infinite number of layers.
1. By separation with a pipet or siphon.	1. By observation along a column.
2. By separation with a mechanical slicer.	2. By observation of the blurring of a boundary.
3. By the use of a porous diaphragm for separation in contact with a quiet liquid.	3. By the use of a porous diaphragm in contact with a stirred liquid.

different finite layers is determined as the process is brought to an end.

B. Experiments in which the diffusion is followed by continuous or intermittent observation, in one or more infinitely thin layers, without disturbing the diffusion process.

Table 2 has been prepared to show some of the kinds of diffusion experiments which have been used.

While it will not be possible to include a complete survey of diffusion apparatus and methods, a few representative examples will be given to illustrate the various types of experiment. Because of the variation of diffusion rate with temperature, and the necessity of avoiding a temperature gradient in the solution itself, it is apparent that the temperature must be accurately controlled during any diffusion experiment. Obviously some types of apparatus lend themselves more readily to thermostatic control than do others. While no mention will be made of the

various means used to maintain the desired temperature, the importance of its influence must not be overlooked.

Of the first group, the so-called second method of Graham (28) marks the beginning of the quantitative study of diffusion, since the design of the apparatus and the boundary conditions allow a mathematical interpretation of the observations. This experiment, as performed by Graham, consisted of placing 100 cc. of salt solution beneath 700 cc. of water by means of a capillary pipet. A cylindrical glass vessel 152 mm. high and 87 mm. in cross section was used. After a measured time interval, 50 cc. or one-sixteenth of the total solution was removed and the salt content obtained by analysis. Graham recorded the salt concentration found in each of the sixteen layers. Besides salt, Graham used albumin, gum arabic, magnesium sulfate, sugar, and other substances, both in water and in ethyl alcohol.

Later Scheffer (70) modified Graham's apparatus by using a pipet with a stopcock at the top to facilitate introduction and withdrawal of solutions. In addition he used one volume of solution under three volumes of water. This allowed the use of Stefan's tables (79). Concentrations were determined volumetrically.

The apparatus of Scheffer was used by Arrhenius (2), who introduced a mercury layer on the bottom of the flask to assure a flat surface. He added a cork through which he could insert the pipet. This arrangement allowed withdrawal of the solution with less mixing than occurred in former types. Calculations were based on Stefan's tables and concentrations were measured analytically.

The diffusion vessel was further improved by Oeholm (62), who placed a stopcock in the bottom through which mercury could be drawn and liquids emptied, and an air vent in the top. The vessel had a greater length to diameter ratio than the older types. The concentrations were determined volumetrically and Stefan's tables were used in calculating the results. Other experimenters to use this apparatus were Herzog and Polotsky (34), who studied the diffusion of dyes, and Jander and Schulz (38), who determined the molecular weight of potassium tantalate and other amphoteric oxyhydrates.

A slightly different form of Graham's apparatus was used by Svedberg (82). Solutions were admitted and removed through a pipet with side arm. Air pressure was used in the removal of the solutions from the cell. Here again the design was such as to permit the use of Stefan's tables.

An early form of diffusion apparatus was that of Fick (18), who made diffusion measurements by immersing a series of cylindrical tubes to half their length in a saturated salt solution. The upper half was then filled with water. The progress of diffusion was measured by means of an

hydrometer. Griffin (29) altered this method slightly by placing several tubes through a partition which divided the upper and lower halves of a box-like container. One medium was placed in one compartment and the other in the second compartment. The partition served to separate solution and solvent except inside the tubes where diffusion took place.

In order to avoid the inevitable mixing which occurred at the beginning of the experiment when the solutions of different concentration were placed in contact with each other, and again at the conclusion of the experiment when the different layers were segregated, various forms of mechanical "slicers" were introduced.

Schuhmeister (72) originated the inverted cylinder method which was later refined by Dummer (16). The diffusion column was built up of two cylinders, one inverted over the other. The diffusing solution was placed in a lower cylinder. The solvent was contained in a similar cylinder which was inverted and placed on a sliding frame. The inverted cylinder was then slid over the first one and the diffusion allowed to start. On completion of the diffusion experiment the frame was slid back again and the contents of the cylinders analyzed.

A distinct type of diffusion cell was devised by von Wogau (97) for use with more viscous solutions. It consisted of eight glass plates with a 2-cm. hole in the center of each. These plates fitted into a frame and, when the holes were lined up, formed a diffusion column the layers of which could be removed at will. It was used to measure the diffusion of zinc, cadmium, lead, tin, and tantalum into mercury. Oehlm (63) adapted this apparatus to the use of the Stefan tables by using four plates. These plates were constructed of brass and carefully ground to insure a perfect fit. Any plate could be removed at will and the solution in it analyzed. This type of apparatus gave more consistent results per layer than the older forms and could be used for viscous liquids and colloidal solutions. Much of Oehlm's diffusion data were obtained with this apparatus.

The diffusion cell described by Cohen and Bruins (12) consisted of six glass plates, the first and sixth acting as bottom and top, respectively. The four middle plates had three 2-cm. holes bored through them. These holes were so spaced that three diffusion columns were formed when the holes were lined up. The diffusing substance was placed in the second plate (from the bottom) and water was placed in the three above it. Additional holes in the plate above allowed the cylinders formed to be filled completely with water or solution. By rotating the plates the water could be slid over the solution. After the diffusion had progressed for the desired length of time, the four layers were separated by merely rotating the plates. Vibration was minimized by the use of a Julius suspension. Concentration was determined by means of an interferometer.

Another type of diffusion system to which mechanical slicing may be applied is that of diffusion into a gel. In this connection the gel will be considered merely as a part of the diffusion apparatus, in so far as its presence offers a solution to several experimental difficulties. With the diffusion taking place in the gel it is possible to get a sharper boundary surface, the danger of mixing is negligible, there is greater freedom from convection currents, and effects due to vibration or other outside disturbances are minimized. The layers may be separated by slicing the gel at the desired points at the conclusion of the experiment. Adsorption of the diffusing molecule by the gel substance and impurities in the gel introduce complications into its use. Further, the assumption that the gel exerts no influence on the rate of diffusion may be open to question.

Graham (28) experimented with gelatin in an apparatus similar to the one that he had used for solutions. One hundred cubic centimeters of 2 per cent gelatin containing 10 per cent sodium chloride was allowed to cool and set in a cylindrical vessel. This was covered with 700 cc. of 2 per cent gelatin and the diffusion allowed to proceed. After several days the gel was removed and cut up into sixteen equal layers for analysis.

Bechhold and Ziegler (4) modified Graham's method by allowing diffusion to take place from the liquid above into the gel. They gauged the concentration by noting the intensity of color of the diffusing substance, by the formation of precipitates in the gel, or by analysis. Stiles and Adair (81) and Stiles (80) used a similar method, allowing the diffusion to proceed from a large quantity of solution upward into narrow glass tubes filled with the gel.

Herzog and Polotsky (34) carried out a large number of experiments on the diffusion of dyes in 5 per cent gelatin where the dye served as its own indicator. Fricke (21) has developed a micro slicing method to study diffusion in agar gels. Ricketts and Culbertson (69) suspended a cylinder of agar gel in a large volume of stirred solution. After diffusion had taken place for a suitable length of time, the gel was removed and sections taken for analysis.

A distinct type of diffusion experiment is that in which the solutions are separated by a porous diaphragm. The diffusion gradient is confined to this porous membrane and the pores may be considered as miniature diffusion columns.

The glass diaphragm method used by Northrup and Anson (60) and later by McBain and Liu (51) has the advantages of speed and simplicity. The apparatus consisted of a sintered glass membrane or alundum disc which separated the two solutions. The more concentrated solution was placed above, thus as diffusion proceeded gravity tended to keep the

solutions at a uniform concentration. At the conclusion of the experiment the solution was withdrawn and its concentration determined.

After an adequate mathematical treatment was formulated, it became possible to consider the solution as a series of infinitely close layers. The types of apparatus used in this case are designed primarily to fulfill the boundary conditions and differ according to the method used in determining the concentration over the system.

The electrical methods may be readily adapted to the measurement of concentration along a column in systems containing electrolytes in solution. Weber (91) arranged a cell in such a way that the potential difference between a metal and its ion in the different layers of a diffusing solution could be measured. He also measured the conductivity between two boundary layers as the material diffused. Procopiu (68) extended Weber's method by introducing a third electrode high in the aqueous layer in order to increase the accuracy of the measurement of concentration difference. Haskell (30) measured the conductivity between pairs of electrodes spaced at intervals along his diffusion column.

Clack (9) based his method on the difference in weight between a saturated solution and the same solution after some of the solute had diffused out. A vessel containing salt solution, immersed in a large volume of pure water, was suspended from a balance arm and the loss of weight with time was recorded.

The possibility of a relationship between the refraction of light and the concentration of diffusion layers was early shown by Wollaston (98). Wild and Simmler (95) derived a mathematical relationship between the refractive index and the concentration of the different layers. The first experimental apparatus for measuring diffusion and heat conduction by means of the refraction of light was devised by Wiener (94). He used a solution, covered with water, in a proper optical vessel. Light of definite wave length was passed through a slit and lens system and into the solution. The interference bands were recorded on a photographic plate as the diffusion progressed. The distance that the center of the light band was deflected by the diffusing solution was measured by means of a cathetometer. Wiener derived the relationship between concentration and the displacement of the light band. Thovert (85) improved Wiener's experiment by using a better source of light with collimator, and by changing the angle of the slits. Later Thovert (86) arranged his apparatus in the form of a spectrometer and measured the deviation by means of an ocular with a movable and fixed crosshair. Variations of Wiener's method have been used by Heimbrodt (31), by Clack (10), and by many others.

An apparatus for the microscopic measurement of diffusion was introduced by Westgren (92) for an investigation of gold and selenium sols.

His cell consisted of a microscope slide and cover glass. The sol was thrown to the bottom of the cell by centrifugal force, the apparatus was placed under the ultramicroscope, and the progress of the diffusion was measured by counting the number of particles at different heights over suitable time intervals. Sitte (74) has used a cross-ruled microscope slide for noting the movement of particles of a gold hydrosol.

When two solutions of different concentrations, either molecular or colloidal, are placed in contact without mixing, a sharp boundary is present between them. As diffusion progresses, however, this boundary becomes blurred, and a concentration distribution is obtained which varies with the distance from the boundary.

Svedberg (83, 84) has made very effective use of this boundary blurring as a means of measuring the diffusion coefficients of proteins. In addition to its use in the ordinary type of experiment he has been able to show that the blurring of boundaries in systems subjected to vibrationless centrifugal fields was a result of diffusion, enabling him to evaluate the diffusion coefficient from its quantitative observation as the centrifuging is continued. The registration of the progress of the diffusion was obtained photographically. This is possible because protein materials fluoresce under the influence of ultra-violet light. The relationship between intensity of fluorescence and concentration of the protein must have been obtained previously by independent experiments in order that the variation of concentration with height in the diffusing column may be made available. Lamm (46) has applied the refractive index method to the study of the blurring of the boundary in the ultracentrifuge.

A microscopic arrangement to measure the diffusion of dyes, using the blurring of the boundary method, was designed by Fürth (25). The diffusion apparatus consisted of a divided cell, the diffusion taking place in the left side. A colorimetric standard was located in the right side. As the diffusion proceeded the microscope was successively focused on the layer whose concentration was comparable to that of the standard solution. The rate of diffusion was determined from the observation of the position of this layer as a function of time. A sharp boundary was obtained by means of a metal partition between the two layers which was removed by means of an electromagnet at the start of the diffusion.

The measurement of diffusion between a stirred liquid and a solution contained in a porous solid offers the experimental advantages of being little affected by vibration or convection currents and of giving a sharp boundary between the two solutions.

Friedman and Kraemer (23) have utilized this method in their investigation of gel structure. In a typical experiment a firm gel was formed in the bottom of a 500-cc. bottle and an equal depth of liquid introduced over

the gel. Either the liquid or the gel contained the diffusing substance at the start of the experiment. The liquid was kept at a uniform concentration by constant stirring. Its concentration was determined at suitable intervals by means of an immersion refractometer. This method of measuring diffusion is also being used by the authors in the investigation of the capillary dimensions of porous solids. The diffusion cell consists of a water-tight brass cylinder provided with a stirrer. After the pores of the solid have been filled with solvent or solution the solid is fitted into the cell in such a way that only the top surface is exposed. An equal depth of either solution or solvent is placed over the solid and maintained at a uniform concentration by stirring.

III. INTERPRETATION

The ability of a substance to diffuse is frequently mentioned and made use of in connection with other and perhaps better known phenomena. Nevertheless, the diffusion of substances in solution is one of the most fundamental of properties, since it is so closely related to molecular motion. The specific diffusion rate or diffusion constant obtained from its study is a valuable constant, since from it much useful information may be obtained. It has found repeated application in both scientific and technical problems. Among the former may be mentioned the determination of molecular and particle size, the development of electrolytic solution theory, the relation between diffusion rate and the velocity of heterogeneous reactions, and the description of the coagulation of colloidal systems in terms of a time constant whose magnitude depends upon the ability of the particles to diffuse.

Reasons have been suggested why diffusion studies have not been made to an extent which seems to be commensurate with their importance. The experimental difficulties involved and the fact that under different conditions inconsistent values result for the diffusion coefficient are undoubtedly the most important of them. Failure of Fick's law and a variation of the coefficient with concentration are frequently mentioned in connection with the second difficulty, and it is indeed unfortunate that these anomalies persist into such low concentrations that only measurements of highest precision permit the estimation of the proper corrections by extrapolation to zero concentration. But in spite of this situation, means are being found to conduct and interpret the experiments in a manner which leads to a consistent result and the information obtained bids fair to repay the extra effort involved.

A. DIFFUSION AND MOLECULAR RADIUS

As we have seen in an earlier section, kinetic theory leads to the expression

$$D = \frac{RT}{N} B = \frac{RT}{Nf} = \frac{RT}{N} \cdot \frac{1}{6\pi\eta r} \quad (27, 28)$$

where f is the reciprocal of the mobility and therefore the frictional coefficient. For a sphere obeying Stokes' law, it is equal to $6\pi\eta r$. Many attempts have been made at a direct experimental confirmation of this law, so that it may be used for the study of the size of molecules. It is a method which should be of considerable value for spherical or nearly spherical molecules, provided the validity of the equation can be established; but unfortunately a rigorous proof of it in such cases does not seem possible. Several methods of test have been recorded in a number of places, and a great deal of experimental work has been done to try to establish it. The more important types of experiment have sought to prove one of the following relationships.

1. In the same solvent and at the same temperature with a number of diffusing substances there should result

$$D \cdot r = \text{const.}$$

2. At constant temperature a given substance diffusing in a variety of solvents should give

$$D \cdot \eta = \text{const.}$$

3. At constant viscosity a substance diffusing at several temperatures should obey the relation

$$\frac{D}{T} = \text{const.}$$

provided the radius of the molecule can be assumed independent of temperature.

Experiments made to test these relationships have usually been as successful as one could reasonably expect. In the very careful experiments of Cohen and Bruins (13) the velocity of diffusion of tetrabromoethane into tetrachloroethane at temperatures ranging from 0°C. to 50°C. was determined, making corrections for the change in the viscosity of the solvent as the temperature was increased. The results of the work are summarized in table 3.

Cohen and Bruins interpret their data to indicate small deviations in the Stokes-Einstein law, but we should prefer to consider these results as a demonstration of the fundamental correctness of the third relationship, considering that the diffusing molecules are not spherical, and that the discontinuities of the medium are not particularly small compared with their size.

To mention a single other example Scheffer and Scheffer (71) studied the temperature dependence of the diffusion constant of mannite in dilute aqueous solutions from 0°C. to 70°C. and found good agreement with the Stokes-Einstein formula. Correcting for the change in viscosity caused by the increase in temperature, the relation $D/T = \text{const.}$ is quite exactly obeyed. The radius of the mannite molecule was calculated to be $r = 4 \times 10^{-8}$ cm.

The proof of the relation $D \cdot r = \text{const.}$ involves the study of the diffusion of a number of different molecules of known dimension in the same solvent and at the same temperature. Among others, Thovert (85, 86, 87) and Oeholm (62, 64, 65) have made studies of just this kind, the former using water and methyl alcohol, and the latter water and ethyl alcohol, as solvents. The variety of solutes used is suggested by the list of materials which were allowed to diffuse into water by Oeholm, as follows: glycerol, pentaerythritol, mannite, alloxan, resorcinol, hydroquinone, saligenin, inulin, acetamide, carbamide, dicyandiamide, caffeine, eegonine, salicin,

TABLE 3
Diffusion data for tetrabromoethane in tetrachloroethane

	TEMPERATURE					
	273.1°C.	283.1°C.	288.1°C.	298.1°C.	308.1°C.	323.1°C.
η	0.0266	0.0215	0.0195	0.0164	0.0140	0.0113
$r \times 10^8$ cm.....	2.15	2.15	2.16	2.17	2.19	2.21

gum arabic, and starch. It is at once apparent that they could not have expected to verify the relationship in question with their experiments because sufficient data concerning the dimensions and shape of these molecules were not available to them. Rather it was their purpose to study the validity of another equation which might appear to have similar significance, namely,

$$D\sqrt{M} = \text{const.} \quad (39)$$

where M is the molecular weight of the solute. This relationship may be obeyed by limited numbers of similar molecules, but consideration of the factors involved makes it at once evident that it cannot have general validity. The reason is just the thing we believe but are still attempting to prove, namely, that the diffusion rate of a molecule is determined by its (effective) radius.

It is the opinion of the writers that the numerous attempts to prove the second equation, $D\eta = \text{const.}$, have not been as successful as they might have been had the several investigators taken care to choose their systems

so that the discontinuities of the medium were small compared with the size of the diffusing solute. The viscosity needed in this equation should be a "microscopic" viscosity and should measure the frictional resistance of the solvent molecules to the linear displacement of the diffusing molecules. Further, there is sometimes considerable doubt as to whether the viscosity as measured in a viscometer and determined by the rate at which the molecules of the medium slip past each other is actually the viscosity that one should use for the required resistance to the displacement of solute molecules. Perhaps the most satisfactory source of information for the present status of the equation involving the coefficient of viscosity is the comparatively recent article of Dummer (16). The results of experiments with acetone, nitromethane, nitrobenzene, ethyl acetate, and ethyl benzoate molecules diffusing into a number of common organic solvents are recorded there.

Remarkable as it may seem, the agreement between theory and fact is often closer and more satisfactory for colloidal systems than it is for ordinary molecular solutions. Measurements on Faraday gold sols having particles of known radius have been carried out by Svedberg (82) in order to test the kinetic formula; he found the particle size calculated by the Stokes-Einstein equation from the diffusion constant to agree within the limit of experimental error with the known radius which had been determined ultramicroscopically, using the Zsigmondy nuclear method. In a representative experiment diffusion gave $r = 1.29 \times 10^{-7}$ cm., and the ultramicroscopic result was $r = 1.33 \times 10^{-7}$ cm. Westgren (93), working in Svedberg's laboratory, carried out a number of similar diffusion measurements with gold and selenium sols, using a method in which a very thin layer of the diffusing solution was placed under a high column of dispersion medium. After a definite period of time the concentrations c_1 and c_2 were determined at the heights X_1 and X_2 . It follows from equation 14 that the concentration ratio may be written,

$$\frac{c_2}{c_1} = e^{-\frac{(x_2^2 - x_1^2)}{4Dt}} \quad (40)$$

thus the diffusion constant can be determined with comparative ease. The concentrations were determined by counting the number of particles at different heights with the ultramicroscope. The values of the radii calculated with the Stokes-Einstein equation agreed very well with the radii determined by other methods.

The consensus of opinion appears to be that the kinetic theory equation can be applied to the determination of molecular sizes if the limitations imposed upon its use are properly recognized. This is a conclusion of great importance because it makes possible the calculation of the equiva-

lent radii of dissolved particles varying in size from quite small molecules to particles of ultramicroscopic dimension. Such work has been done by Herzog and his collaborators (32, 34), who have studied the diffusion behavior of and calculated the particle size for cellulose esters, rubber, proteins, ferments, and dyes in their proper solvents. More recently Fürth and his associates (25) have developed and used a rapid micro method which permits an estimation of the particle size of dyestuffs in solution.

Svedberg (84) makes very ingenious use of diffusion coefficient determinations in connection with his sedimentation velocity method for the determination of molecular radius and weight. By combining the results of the two studies, made simultaneously in the ultracentrifuge, and by assuming that the frictional resistance exerted by the solvent in diffusion is equal to the frictional resistance, which determines the sedimentation velocity, the equations describing each phenomenon can be combined to eliminate the friction term, giving,

$$M = \frac{RT \ln (x_2/x_1)}{D (1 - V\rho) \omega^2 (t_2 - t_1)}, \quad (41)$$

where M is the molecule weight of the solute,

x_1 and x_2 are distances between the axis of revolution and the boundary at times t_1 and t_2 ,

ω is the angular velocity of the rotor of the centrifuge,

V is the partial specific volume of the particle,

ρ is the density of the solvent, and

D is the diffusion coefficient.

The diffusion constant, which must be determined separately, is obtained from the blurring of the boundary as it recedes. The purpose of this method of procedure is to eliminate the use of Stokes' law to evaluate the frictional resistance to the motion of the particles, involving as it does certain undesirable conditions for validity.

In an extremely interesting table which is here reproduced (table 4), Svedberg (84) has compared values of molecular radii for a number of proteins calculated from sedimentation velocity studies with those determined using diffusion measurements. In certain cases the values of the radius obtained by the two methods are in excellent agreement, indicating a spherical shape for their molecules, but in others there is considerable difference, a result of the failure of the Stokes-Einstein law when it is applied to nonspherical molecules.

In the attempt to accelerate and simplify diffusion methods as applied to biological materials, Northrup and Anson (60) have resorted to the use of a thin porous plate to make the concentration gradient high and at the

same time to avoid convection currents. Thus the pores of the diaphragm must be small enough to prevent convection and at the same time large enough to allow free diffusion. The apparatus, after calibration with a hydrochloric acid solution, was used to study the diffusion rate of hemoglobin. Using the Stokes-Einstein law it was found to have a molecular weight of $68,500 \pm 1000$, which agrees "within the experimental error with that of 67,000 found by Adair by osmotic pressure measurements and of 68,000 found by Svedberg from experiments on the rate of sedimentation." In using the Stokes-Einstein equation, it was assumed that the hemoglobin molecules are spherical and impelled by a force given by an idealized osmotic pressure law against a resistance as given by Stokes' law. But Svedberg has shown in quite convincing manner (table 4) that hemoglobin molecules cannot be spherical. Using Einstein's law, Sved-

TABLE 4
Molecular radius data for protein molecules

MOLECULE	SPECIFIC SEDIMENTATION VELOCITY AT 20°C.	DIFFUSION CONSTANT AT 20°C.	r (SEDIMENTATION VELOCITY)	r (STOKES-EINSTEIN)
	<i>cm. per second</i>	<i>cm.² per second</i>		
Egg albumin.....	3.32×10^{-13}	9.58×10^{-7}	2.18	2.23
Hemoglobin.....	4.37×10^{-13}	6.36×10^{-7}	2.44	3.35
Serum albumin.....	4.21×10^{-13}	6.10×10^{-7}	2.39	3.49
Serum globulin.....	5.57×10^{-13}	5.40×10^{-7}	2.75	3.96
Phycocyan.....	5.59×10^{-13}	5.28×10^{-7}	2.76	4.04
Phycocerythrin.....	11.30×10^{-13}	5.22×10^{-7}	3.93	4.09
Limulus-hemocyanin.....	35.50×10^{-13}	1.87×10^{-7}	6.96	11.40
Helix-hemocyanin.....	98.00×10^{-13}	1.78×10^{-7}	12.00	12.20

berg calculated the radius of the hemoglobin molecule to be 3.35×10^{-7} cm., while Northrup and Anson gave 2.73×10^{-7} cm. for the same constant. It is true that Svedberg's experiments were made at 20°C., or 15°C. higher than those of Northrup and Anson, but it is difficult to see how this difference in radius could be accounted for on this basis alone.² One must therefore feel that results obtained in this way for a diffusion constant or radius can only be accepted as provisional until independent confirmation of the method can be obtained. It is true that McBain and Liu (51) have given a simple and rapid procedure for the use of the Northrup diffusion cell, in which it was shown that the results are independent of the nature and porosity of the diaphragm and equivalent to the best obtained by the more laborious classical methods.

² Note added in proof: Tiselius and Gross (Kolloid-Z. **66**, 11 (1934)) have shown that the diffusion constant varies with the concentration of solute. Their data make possible an explanation of this difference.

B. DIFFUSION AND ELECTROLYTIC SOLUTION THEORY

It has been seen in an earlier section of this report that an independent diffusion of ions is impossible because of the electrostatic forces between them; thus the problem is more complex than the one involving neutral molecules alone. However, Nernst (57) was able to show that the amount of salt diffusing in a given time could be expressed in terms of the mobilities of the ions, the cross-sectional area of the diffusing medium and the concentration gradient, when 100 per cent dissociation can be assumed. Important experimental studies of the diffusion coefficients of salt solutions have been carried out by Haskell (30), Oeholm (62, 64), Clack (10), McBain (50, 51), Sitte (75), and others. In the verification of the interionic attraction theory of diffusion due to Onsager and Fuoss (66), it is preferable to utilize differential coefficients of diffusion rather than those obtained by allowing a given solution to diffuse into pure solvent, but comparatively few data of this type are available. Those of Clack which meet this particular requirement were made in a concentration region from 0.05 *N* to saturation, so they hardly permit a test of the theory in the region where the interionic effects predominate. The Onsager theory does account for the general type of the relation between the diffusion constant and concentration, but there are difficulties which must still be overcome. Onsager and Fuoss have discussed this situation in great detail, therefore further reference to it here is unnecessary. We may venture to predict that when precision measurements designed for the express purposes of the theory have been made, the situation will have been considerably improved.

Haskell has studied the interesting and practically important case of a dissociating solute which diffuses in the two parts,—the dissociated and the undissociated. He could show in the first place that the diffusion constant generally becomes larger as the dilution is increased, which is interpreted to mean that the ions move more rapidly than the undissociated portion. The problem Haskell set for himself was to see if during an infinitesimal time these parts could not be considered as moving independently, each having its own diffusibility, so that the total amount of material dm crossing a given area is

$$dm = dm_1 + dm_2$$

where dm_1 represents an amount of unionized salt, and dm_2 represents an amount of ions. The complex differential equation necessary to describe the problem could not be solved directly so that the approximate methods of procedure suggested in Part I were resorted to. Experiments with thallium sulfate and barium nitrate in tenth-normal solution led to the conclusion that the rate of diffusion of the undissociated molecules is of the magnitude one-half that of the ions.

In order to test the Nernst formula, Oeholm investigated the diffusion of a number of strong electrolytes of valence type 1-1 in water solution at concentration 0.01 *N* and found substantial agreement. A portion of the data are collected to form table 5.

The relation between the mobility of the ions under the influence of an electrical field and their ordinary diffusion is therefore justified. The Nernst expression has been generalized by Noyes, who has applied it to the case in which a salt is completely dissociated into any number of ions. This extension is given in detail in the article by Haskell.

TABLE 5

Diffusion of simple electrolytes in dilute aqueous solution at 18°C.

ELECTROLYTE 0.01 <i>N</i> IN WATER	<i>D</i> (OBSERVED) OEHOLM	<i>D</i> (CALCULATED) NERNST
NaCl.....	1.170	1.173
KCl.....	1.460	1.460
LiCl.....	1.000	0.994
KI.....	1.460	1.467
HCl.....	2.324	2.431
NaOH.....	1.432	1.558
KOH.....	1.903	2.109

C. DIFFUSION AND HETEROGENEOUS REACTION KINETICS

The dissolution of a substance, whether it be a salt dissolving in water, a metal dissolving in an acid, a resin dissolving in acetone, etc., naturally has been the subject of much study. The classical theory for the rate of solution of solids due to Noyes and Whitney (61) and to Nernst (58) has postulated that the rate of this process is very high compared to the rate at which the active component of the solution can reach the solid surface by diffusion, hence the solution rate should be dependent upon that of the diffusion to the surface through the products as they are formed and diffusing away from the surfaces being attacked. However, van Name and Hill (89) and others have recognized that this theory can not be as generally applicable to heterogeneous reactions as had previously been supposed. There are now generally assumed to be three types of heterogeneous reaction, provided that we exclude certain other complicating factors which would certainly interfere, as follows:

1. Those in which the surface reaction is very much faster than the diffusion rate, the observed reaction rate being determined by the latter.
2. Those in which the reaction is very slow compared to the diffusion rate, the latter then being without influence in determining the rate of the process.

3. Those in which the diffusion rate and reaction rate are comparable in magnitude, so that both factors will influence the observed reaction rate.

Interest in this problem has been revived because of the work and discussions of Brönsted and Kane (7), Kilpatrick and Rushton (41), and King and Braverman (42) on the rate of solution of metals in acids. It will be recalled that Nernst (59) had postulated the existence of a "diffusion layer" surrounding the solid, the thickness of which could be calculated from the expression,

$$k = \frac{D}{\delta} \quad (42)$$

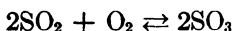
where k is the observed solution rate, D is the diffusion coefficient, and δ is the thickness of the layer. Thus, if the thickness of the adhering layer for a given kind and velocity of stirring can once be determined by experiment, the velocity constant of the reaction can be calculated. This constant could be obtained by Brunner (8) from measurements on the rate of solution of magnesia in benzoic acid, after which it was possible to calculate the rate of solution of magnesia in a number of different acids. A further conclusion seems to follow at once: it is not the strength of the acid which regulates the rate of attack, but rather the diffusion coefficient. Further results of experimental work in general agreement with this conclusion have been published by van Name and his associates (88), and by Heymann (36). They all dealt with typical cases in which no other slow processes were involved, so that reasonably good agreement must have been expected.

But while the process of solution of metallic oxides, hydroxides, and carbonates in acids may be so rapid that the observed rate of solution may be controlled by the diffusion process, it could well be that the chemical reaction involved in the dissolution of metals in acids will be slower than the accompanying diffusion. Brönsted and Kilpatrick have therefore begun such experimental studies to determine whether, as heretofore supposed, only the hydrogen ion reacts directly with the metal, or whether other acid ions and molecules enter into such reactions as well. To quote Brönsted and Kane, "There is no reason, however, to assume that the reaction of dissolved molecules with the molecules of a solid substance should be instantaneous or in any way more rapid than the reactions of dissolved molecules between themselves. The diffusion theory is therefore inapplicable for a general explanation of heterogeneous reactions. On the other hand, when the elementary reaction proceeds with sufficient rapidity, there is no doubt that the diffusion of the reacting acid to the interface plays a part more or less important for the dissolving process."

The work of Brönsted and Kilpatrick attempts to deal with the subject from the standpoint of the extended theory of acids and bases, now well known as the result of work by Brönsted and by Lowry. Kilpatrick and

Rushton have observed the rate of dissolution of magnesium in various acids and buffer solutions with results which have to be interpreted to mean that the chemical process is much slower than the diffusion process. In a more complete work Brönsted and Kane have applied this theory to the rate of solution of sodium from sodium amalgam by acids, in which it is concluded that while the diffusion process determines the rate with the stronger acids, the chemical reaction rates are sufficiently lower than the diffusion rates in the case of acids of dissociation constant less than 10^{-7} to be responsible for the observed velocities. King and Braverman, on the other hand, are not convinced of the sufficiency of the arguments which have led to these conclusions. They point out five criteria which are generally accepted for the validity of the "diffusion rate" theory, and insist that neither Kilpatrick and Rushton nor Brönsted and Kane have tested their detailed application. Their own studies on the rate of solution of zinc in acids lead to certain results which are definitely contradictory to the Brönsted-Kilpatrick explanation; at the same time they recognize that the older diffusion rate theory cannot be applied to their data without some modification. Further investigation of these problems will undoubtedly be forthcoming.

The theory of the rate of gaseous reactions at the surface of catalysts has been subjected to similar transitions. A number of individual reactions can not be discussed in the space available to us, but it will be of interest to suggest the changes in viewpoint as to mechanism which one reaction chosen as typical of them has undergone. The reaction chosen is that of the contact sulfuric acid process,



In the attempt to explain the observed rates of this reaction under different experimental conditions, Bodenstein and Fink (5) made use of a modification of the Nernst theory of heterogeneous reactions described above. In other words, they assumed that these rates were determined by the rate at which the reacting gases diffused through a film of gas adsorbed on the surface of the catalyst. The mathematical formulation was complicated by the retardation of the reaction by the sulfur trioxide formed in the reaction; nevertheless two expressions could be set up depending upon whether the oxygen or sulfur dioxide was present in excess.

(1) SO_2 in excess:

$$\frac{d[\text{SO}_3]}{dt} = k \frac{[\text{O}_2]}{[\text{SO}_3]^{\frac{1}{2}}} \quad (43)$$

(2) O_2 in excess:

$$\frac{d[\text{SO}_3]}{dt} = k \frac{[\text{SO}_2]}{[\text{SO}_3]^{\frac{1}{2}}}$$

Thus, the reaction velocities depend upon the diffusion of oxygen if sulfur dioxide is present in excess and upon the diffusion of sulfur dioxide if oxygen is present in excess, again provided the rate of reaction at the surface is rapid with respect to the diffusion. The term $\frac{1}{[\text{SO}_2]^2}$ is empirical in nature.

There are several serious objections to this explanation. As Langmuir (48) has pointed out, to account for the slowness of this and similar reactions it would be necessary to assume the existence of retarding layers of such thickness that they would be visible. Furthermore, the high temperature coefficient of surface reactions is inconsistent with the much slower variation of a diffusion rate with temperature. Because of these and other difficulties Langmuir was led to seek another explanation, and in a remarkable paper published more than ten years ago he was able to develop an entirely new theory for the kinetics of such reactions, based upon his interpretation of evaporation from and condensation on solid surfaces. According to it the rates of evaporation and condensation are determined by the nature of the forces operative between the solid and gas and the number of active spots available on the surface. The forces involved, which are of chemical nature, are limited in range to distances of the order of molecular thicknesses. The adsorption on the surface is the result of a time lag between condensation and evaporation. Two general cases are considered.

1. Surface of catalyst only slightly covered by monomolecular layer.
2. Surface of catalyst practically completely covered by reacting gases.

The interesting thing for our purpose is that deductions based upon the "monomolecular layer" theory lead to reaction rate equations which are identical in form with those found by Bodenstein and Fink, and for which a diffusion mechanism was postulated. Once more, then, we are faced with the necessity of a differentiation between monomolecular and polymolecular theory. The presumption is decidedly in favor of the monomolecular theory at the present time.

D. DIFFUSION AND KINETICS OF COAGULATION

In the field of homogeneous reaction kinetics the bimolecular reaction has been successfully described by a collision mechanism based upon kinetic theory. The expression for the specific reaction rate of such a reaction is,

$$k = se^{-\frac{E}{RT}} \quad (44)$$

where s is the number of molecules colliding, and $e^{-\frac{E}{RT}}$ is a numeric representing the fraction of the molecules having energy equal to or greater than

the activation energy E . In short, the reaction occurs when activated molecules collide. A similar problem presents itself when we come to study the problem of the coagulation of a colloidal system, which, with respect to the rate of change of the total number of particles, is equivalent to a polymerization reaction of the second order. The solution of this problem was shown by Smoluchowski (77) to be comparatively simple in the case of a rapid coagulation, but it is more complex for slow coagulation.

In considering the coagulation process, two factors must be carefully differentiated. In any colloidal system there is always a definite probability of collision between particles, and there is further a definite probability of adhesion, once collision has taken place. By rapid coagulation is meant that process taking place when the probability of adhesion approaches unity, or when all collisions are effective in reducing the total number of particles. When the probability of adhesion is less than unity, the coagulation is characterized by the word "slow." The quantitative relations for rapid coagulation in a dispersion of spherically shaped particles of uniform size are based upon the assumption that two particles adhere whenever they diffuse to within a certain distance R , which is slightly more than twice the radius of a single particle. These relationships provide an answer to several questions, as follows:

1. The change in the total number of particles,

$$N = \frac{N_0}{1 + \frac{t}{T}} \quad (45)$$

2. The change in the number of single particles,

$$N_1 = \frac{N_0}{\left(1 + \frac{t}{T}\right)^2} \quad (46)$$

3. The change in the number of double particles,

$$N_2 = \frac{N_0 \left(\frac{t}{T}\right)}{\left(1 + \frac{t}{T}\right)^3} \quad (47)$$

4. The change in the number of particles of k -order,

$$N_k = \frac{N_0 \left(\frac{t}{T}\right)^{k-1}}{\left(1 + \frac{t}{T}\right)^{k+1}} \quad (48)$$

In these equations, N , N_1 , N_2 , N_k are the numbers of all, single, double, and

k^{th} -order particles, respectively, at time t ; k is the number of primary particles in the aggregate; N_0 is the number of particles at the start of the experiment; and T is a constant characterizing the rate of coagulation.

The constant T is of special interest because it is theoretically equal to $\frac{1}{4\pi N_0 D R}$, with D the diffusion coefficient. The constant D is involved because it determines the frequency with which collisions between particles can occur. The probability that one particle considered as stationary in a sol containing N_0 particles per cubic centimeter will be struck by another is

$$P = 4\pi D R$$

Thus, starting with N_0 particles, the number remaining after time t will be

$$N = N_0 e^{-4\pi D R N_0 t} \quad (49)$$

The derivation of the several equations given above follows directly from this statement. The similarity with the expression which describes the bimolecular reaction is now made apparent.

In actual practise the constant T is determined empirically by noting the time at which the total number of particles has fallen to one-half of its original value. In this manner the theory has been confirmed by direct ultramicroscopic count when the coagulation process could be described as a rapid one.

For slow coagulations the application of the theory after its modification to allow for a definite fractional number of effective collisions has not been so successful. In some laboratories this failure of the theory is believed to be due to a sensitivity of slow coagulation to variations in particle size and to deviations from spherical shape. The situation has been considerably improved by the excellent theoretical work of Müller (53), in which these factors are given due consideration. In spite of its shortcomings the coagulation theory is to be considered another triumph of the molecular kinetic point of view as applied to colloidal systems, and improvements in the present situation may be expected.

IV. APPLICATIONS

Diffusion theory has been shown to be of considerable significance for certain fundamental questions of the purely physical sciences. In addition, the application of diffusion measurements to scientific and engineering problems has been attended with success in a number of instances, so much so that it seems worth while to suggest some of them before concluding this report.

An excellent example of an engineering application is found in the wetting and drying of porous solids of all kinds. The wetting of an insulat-

ing material by absorption of moisture which exerts a profound effect upon its electrical characteristics, has been described by means of the diffusion law in many instances. Thus, Andrews and Johnston (1) have shown that the process of water absorption when a sheet of rubber is immersed in water follows the diffusion law. As was pointed out by these investigators, it is a further consequence of this law that for a given sample of rubber the time required to reach a specified degree of saturation is proportional to the square of the thickness of the sheet, an important result because it enables the prediction of the behavior of thicker sheets from observations made upon thin sheets which become saturated in comparatively short times.

The inverse problem, that of the drying of a solid, has also been the subject of much discussion. As Sherwood³ (73) has pointed out in an interesting series of articles dealing with this problem, the water contained in the solid must by some mechanism travel to the surface before it can escape. It has been generally assumed that it travels through the solid by diffusion as a liquid, although the possibility of its diffusing as water vapor has also been considered. In any quantitative consideration of the problem there must be described the mode of transport of the water through the solid, the place and rate of the evaporation, the distribution of moisture in the solid, and the temperature. In the process discussed by Sherwood it is assumed that the temperature, humidity, velocity, and direction of the air are maintained constant, and that the latent heat of vaporization of the water is received by the solid by convection.

The general mechanisms of drying can be classified as follows:

1. Evaporation of the liquid at the surface of the solid, with resistance to internal diffusion of liquid small as compared with resistance to the removal of vapor from the surface.
2. Evaporation at surface, but with resistance to internal liquid diffusion great as compared to the removal of vapor from the surface.
3. Evaporation in the interior of the solid, with resistance to internal diffusion great as compared with resistance to the removal of vapor.

Observations on the rate of drying of a porous slab as a function of the water content led Sherwood to divide the process into a constant rate period and a falling rate period. During the constant rate period the evaporation takes place at the surface of the wet solid much as it does from the surface of a liquid, with the rate of drying being limited by the diffusion rate of water vapor through the surface air film outward. The falling rate period is shown to be further divisible into two zones, a first one in which the rate of drying decreases because of a reduction in the area of

³ Many other investigators have considered these and similar problems, and although there has sometimes been uncertainty with regard to detail they are essentially in agreement with the views to be described here.

wetted surface, and a second one in which the drying is controlled by internal liquid diffusion, of which either mechanism or each in turn may prevail. It is also true that the less porous materials show no constant rate period at all, the process being controlled entirely by internal liquid diffusion.

The movement of liquids through solids obeys the same fundamental diffusion laws as hold in the case of molecular diffusion in liquid systems, and equations of the form considered in the theoretical section may be applied to the process. Among other things it can readily be shown that the time required to dry to a given water content is proportional to the square of the block thickness, the diffusion taking place in the direction in which the thickness is measured. A further point of interest has to do with the plane from which the evaporation takes place in the second zone of the falling rate period. This plane of evaporation may move inward from the surface or it may remain effectively at the surface, depending upon whether the solid is porous or fibrous as in the case of paper pulp, or whether it is amorphous as in rubber or clay. In this way diffusion studies can give definite information concerning the structure of solids.

In a somewhat different way this statement also may be illustrated by the work of Friedman and those associated with him (22, 23, 43), who have studied the porosity of dilute gels using diffusion measurements. The problem turns on the very slight hindrance that these gels offer to small molecules diffusing through them. Thus the viscosity theoretically related to the diffusion constant is but slightly greater than that of the liquid itself, and the diffusion must take place in the liquid contained in the pores of the gelatin, agar, and cellulose acetate gels which have been investigated.

The decreased diffusion constant is assumed to have resulted from the operation of three factors:

1. A reduction of diffusion space by the volume of the gel structure.
2. An increased resistance to motion due to the proximity of the cell walls.
3. An increased viscosity of the free liquid due to solution of some of the gel substance.

These factors were taken into account using a relationship of the following form:

$$D_w = D_g \left(1 + 2.4 \frac{r}{R} \right) (1 + \pi) (1 + \alpha) \quad (50)$$

where D_w is the diffusion constant of the solute in pure water,
 D_g is that observed in the gel,
 r is the radius of the diffusing molecule,

- R is the average pore radius in the gel,
 π is the correction factor for the mechanical blocking, and
 α is the correction factor for the viscosity.

The correction factor α can be calculated from the difference between D_w and the diffusion constant obtained by extrapolation to zero concentration of the data for the dilute gels. The correction for mechanical blocking, which incidentally will depend upon whether a semicrystalline (fibrous) or amorphous structure is involved, was obtained from a formula given by Dumanski (15) some years ago. The third factor is estimated from Ladenburg's correction (45) for the fall of bodies in a capillary tube. The results of the work with gelatin gels are summarized in table 6. The agreement between pore size values obtained with different diffusing molecules will be observed to be satisfactory; furthermore the values themselves are of the expected magnitude.

The authors of this article have been engaged for some time in similar

TABLE 6
Effective pore size in gelatin gels by diffusion method

DIFFUSING SUBSTANCE	EFFECTIVE PORE DIAMETER		
	5 per cent gelatin	10 per cent gelatin	15 per cent gelatin
	$m\mu$	$m\mu$	$m\mu$
Urea.....	9.4	3.0	1.6
Glycerol.....	11.4	3.4	2.0
Sucrose.....	11.0	2.8	1.0

experiments in which lactose and glycerol have been allowed to diffuse both in and out of soaked blocks of wood arranged in the several directions. The samples used up to the present time have been both the sapwood and heartwood of cedar, western hemlock, and white pine. The effective pore size calculations involve several difficult assumptions; nevertheless, preliminary results are in reasonably good agreement with those of Stamm (78), obtained by other and ingenious methods.

A problem less closely related to our discussions, but one which is of considerable significance, has to do with the diffusion and electrolytic conduction in crystalline solids, the most recent and satisfactory treatments of which have been given by Hevesy (35) and by Jost (39). If it is assumed with Frenkel (20) that in such systems diffusion and electrolytic conduction are the result of migration of the ions in the interlattice space, and of migration of the vacant places themselves, it is possible to account not only for the temperature dependence, but also for the magnitude of these effects

which are known from numerous experiments. In the literature, diffusion and mobility of ions have been represented by a term of the form

$$ae^{-\frac{b}{kT}}$$

in which the constant a depends upon the mobility of a single ion, the ionic concentration, and, in the case of conductivity, the ionic charge, while the constant b determines an energy of liberation required by the ion to leave its normal position.

The applications to physiology and biology are numerous, but necessarily qualitative or semiquantitative in character. Indeed, the complexity of the systems involved is often such that there is difficulty in identifying and segregating the phenomena actually involved. But in spite of this fact much has been accomplished. It was at one time believed that the sorption of materials in biological systems took place as a result of diffusion alone, but the insufficiency of this point of view is recognized, now that negative osmose, selective adsorption, variations in cell structure and composition, and other factors are better understood. Certainly it seems to be true that there is a parallelism between rate of diffusion and the rate of sorption (37, 90). Bechhold (3) and many others (52, 96, 26) discuss diffusion, osmotic pressure, swelling, and shrinking as factors involved in the entry of food into cells and in the circulation of matter. Diffusion is involved in the processes of secretion and excretion, but certainly not in a simple way.

Diffusion studies with enzymes have been made with two objects in view, one in the attempt to obtain a theory for the velocity of enzyme catalysis and the other to separate the enzyme from other crystalloids and colloids. Herzog and Kasarnowski (33) have determined the diffusion coefficients of several enzyme preparations. Fränkel and Hamburg (19) and others have shown that enzyme preparations consist of a diffusible and nondiffusible part; thus enzymatic cleavage may form products which pass into the circulating fluids of an organism by diffusion through membranes. Experiments by Nelson and associates (55, 56), in which the temperature coefficients of enzyme reactions were studied, have led them to conclude that chemical reaction and not diffusion determines the velocity of enzyme catalysis. The study of enzymes from the standpoint of the chemistry of invertase has been reviewed recently in This Journal by Nelson (54).

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THE HOFMANN-BECKMANN-CURTIUS-LOSSEN REARRANGEMENTS

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INTRODUCTION

In this paper the attempt is made to show that the Hofmann, Beckmann, Curtius, and Lossen rearrangements involve the augmentation¹ (1) of primary alcohols to aldehydes, (2) of secondary and tertiary alcohols to ketones, (3) of aldehydes and ketones to carbylic acids,² and (4) of carbylic acids to carbonic acids. The augmenting agents which bring about these rearrangements are hypochlorous acid chlorine, hypobromous acid bromine, nitric acid nitrogen, hydrogen peroxide oxygen, the hydroxylamine NO group, and hydrazine nitrogen.

Alcohols

The mono- and di-alkyl amines are ammonio alcohols, which is to say that they are alcohols belonging to a nitrogen system of compounds in the same sense that the aquo alcohols may be said to belong to an oxygen system (24, 27).

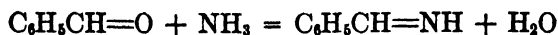
The formulas RCH_2OH , RCH_2NH_2 , and RCH_2NHCH_2R represent primary alcohols; R_2CHOH , R_2CHNH_2 , and $R_2CHNHCHR_2$ secondary alcohols; R_3COH , R_3CNH_2 , and R_3CNHCR_3 , tertiary alcohols; RCH_2NHCHR_2 , mixed primary secondary alcohols; RCH_2NHCR_3 , primary tertiary alcohols; and $R_2CHNHCR_3$, secondary tertiary alcohols.

In support of our assumption that the amines represented by these formulas are just as truly alcohols as are their oxygen analogs, it will suffice present purposes to emphasize the fact that they closely resemble the aquo alcohols in their behavior toward augmenting agents. For example, Chuck (14) found that benzamidine is formed in good yields when a liquid ammonia solution containing benzylamine and ammonium

¹ The terms "augment" and "augmentation" will be used instead of "oxidize" and "oxidation" as understood in the broad general sense (28).

² The carboxylic acids, the carbazylic acids or acid amidines, and the carboxazylic acid or acid amides.

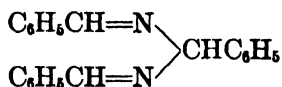
azide is heated at 60°C. for a time; and Strain (71) prepared benzylideneimine by the ammonolytic action of liquid ammonia on aquobenzaldehyde



and found furthermore that benzylideneimine, under the action of iodine in liquid ammonia solution, is readily nitridized to benzamidine.

Aldehydes and ketones

Contingent upon the trivalency of nitrogen in contrast with the divalency of oxygen, strict nitrogen analogs of the aquo aldehydes and aquo ketones are a theoretical impossibility. Approximate analogs of benzaldehyde, for example, are benzylideneimine, $\text{C}_6\text{H}_5\text{CH}=\text{NH}$, phenylbenzylideneimine, $\text{C}_6\text{H}_5\text{CH}=\text{NC}_6\text{H}_5$, and hydrobenzamide,



all three of which closely resemble ordinary benzaldehyde in their aldehydic behavior. All three compounds are aldehydes in so far as the carbon to nitrogen double bonds are concerned. Somewhat arbitrarily perhaps we have chosen to call the first compound a benzaldehyde-alcohol, the second, a benzaldehyde-ether, and the third, a benzaldehyde-acetal. The formulas, $\text{R}_2\text{C}=\text{NH}$ and $\text{R}_2\text{C}=\text{NR}'$, represent ketone-alcohols and ketone-ethers which are the approximate analogs of the aquo ketones. Without forgetting that ethylideneimine and benzylideneimine, by virtue of the presence of the imino hydrogen, are something more than aldehydes, we shall on occasion speak of the former as an ammonoacetaldehyde and of the latter as an ammonobenzaldehyde.

Carbylic acids

Acetic acid, CH_3COOH , acetamide, CH_3CONH_2 , and acetamidine, $\text{CH}_3\text{C}(\text{NH})\text{NH}_2$, are, respectively, an aquoacetic acid, an aquo-ammonoacetic acid and an ammonoacetic acid. With acetic acid and other acids containing the carboxyl group, long familiarly known as carboxylic acids, we have adopted the practice in this laboratory of referring to the acid amides as carboxazylic acids, the acid amidines as carbazylic acids, and of including the carboxylic acids, the carboxazylic acids, and the carbazylic acids under the general designation of carbylic acids.

Carbonic acids

The formula $\text{OC}(\text{OH})_2$ represents an aquocarbonic acid which is assumed to exist in water solution. Cyanamide, H_2NCN , and guanidine,

$\text{HNC}(\text{NH}_2)_2$, are examples of ammonocarbonic acids. Cyanic acid, HNCO , carbamic acid, H_2NCOOH , and urea, $\text{OC}(\text{NH}_2)_2$, are aquo-ammonocarbonic acids (26).

Plus and minus signs

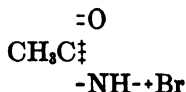
It is fair to assume that all covalent bonds between unlike atoms are more or less polar, which is to say that the one atom of a bonded pair is positive, augmented, de-electronized, with respect to the other. On this assumption we shall on occasion find it convenient to represent this polarity³ by means of small plus and minus signs, as for example in the formulas, CH_3^+-OH and $\text{CH}_3^+-\text{NH}_2$, for methyl alcohol and methylamine. The plus signs are to be read as indicating that the carbon atom in the methyl group is more or less augmented in respect to the hydroxyl and amino groups; the minus sign, conversely, that the oxygen and nitrogen atoms are in a corresponding state of reduction.

Whether belonging to the oxygen system or to the nitrogen system, the primary, secondary, and tertiary alcohols are characterized by the respective groups, RCH_2^+ , R_2CH^+ , and R_3C^+ , the aldehydes by the group, RCH^\ddagger , the ketones by $\text{R}_2\text{C}^\ddagger$, and the carbylic acids by RC^\ddagger . We shall therefore on occasion speak of the augmentation of an alcohol to an aldehyde when, under the action of an augmenting agent, an RCH_2^+ group passes over into an RCH^\ddagger group, of the augmentation of an aldehyde to a carbylic acid when an RCH^\ddagger group is converted into an RC^\ddagger group, and of the augmentation of a carbylic acid to a carbonic acid when the carbon atom of an RC^\ddagger group is converted into a carbonic acid carbon atom, $^\ddagger\text{C}^+$.

In general, the carbylic acids are decidedly stable toward augmenting agents. Even so we shall find as we proceed that certain intramolecular rearrangements are to be explained on the assumption that they involve augmentation of carbylic acids to carbonic acids.

Hypohalous acids

Chloramine, $\text{H}_2\text{N}-\text{Cl}$, and dichloramine, $\text{HN}=\text{Cl}_2$, as nitrogen analogs of aquohypochlorous acid, $\text{HO}-\text{Cl}$, are ammonohypochlorous acids which, like the aquo acid, are effective augmenting agents. Ethylechloramine, $\text{C}_2\text{H}_5\text{NH}-\text{Cl}$, diethylechloramine, $(\text{C}_2\text{H}_5)_2\text{N}-\text{Cl}$, and ethyldichloramine, $\text{C}_2\text{H}_5\text{N}=\text{Cl}_2$, are ethyl esters of the two ammonohypochlorous acids. Acetbromamide, represented by the formula



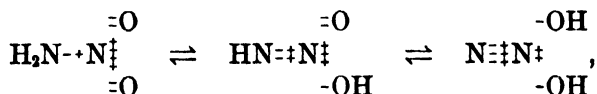
³ Potential polarity according to W. A. Noyes (51).

is a mixed compound which is at the same time an aquo-ammonoacetic acid and an ammonohypobromous acid.

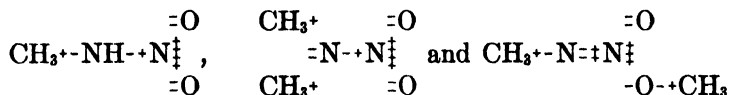
Nitric acids

Ordinary nitric acid, $\text{HO}-\text{N} \begin{smallmatrix} \text{=O} \\ \vdots \\ \text{=O} \end{smallmatrix}$,

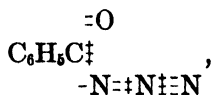
nitramide,



and hydrazoic acid, $\text{HN}=\text{N} \equiv \text{N}$, are respectively an aquonitric acid, an aquo-ammononitric acid, and an ammononitric acid. The formulas



represent known esters of nitramide. Benzyl azide, $\text{C}_6\text{H}_5\text{CH}_2^+-\text{N}=\text{N} \equiv \text{N}$ is a benzyl ammononitrate. Benzoyl azide,



is a compound which is at the same time a mixed benzoic anhydride-anammonide and a nitric acid anammonide, the acid anammonides being the nitrogen analogs of the acid anhydrides.

Hydrazoic acid in all probability is a tautomeric compound to which

either of the formulas, $\text{HN}=\text{N} \equiv \text{N}$ or $\text{HN} \begin{smallmatrix} \text{N} \\ \vdots \\ \text{N} \end{smallmatrix}$, may be ascribed. The first formula represents an ammononitric acid, the second a cyclic nitrous acid hydrazide. The formula,



represents hydrazoic acid, an ammonohyponitrous acid.

Nitrous acids

The following formulas, $\text{HO}-\text{N}=\text{O}$, $\text{HO}-\text{N}=\text{NH} \rightleftharpoons \text{O}=\text{N}-\text{NH}_2$, and $\text{H}_2\text{N}-\text{N}=\text{NH}$, represent an aquonitrous acid, an aquo-ammono-

nitrous acid and an ammononitrous acid. The first acid is known in solution and in the form of salts and esters; the second and third in the form of esters and ester salts. Diazobenzene, $\text{C}_6\text{H}_5\text{--N}=\text{N}^+\text{--OH}$ and dimethylnitrosoamine, $(\text{CH}_3)_2\text{N}=\text{N}^+=\text{O}$, are esters; diazobenzene potassium, $\text{C}_6\text{H}_5\text{--N}=\text{N}^+\text{--OK}$, is an ester salt of an aquo-ammononitrous acid. Diazoaminobenzene, $\text{C}_6\text{H}_5\text{--N}=\text{N}^+\text{--NH}^+\text{--C}_6\text{H}_5$, and diazoaminobenzene sodium, $\text{C}_6\text{H}_5\text{--N}=\text{N}^+\text{--N}(\text{Na})\text{C}_6\text{H}_5$, are respectively an ester and an ester salt of an ammononitrous acid.

Hydrogen peroxide, hydroxylamine, and hydrazine

For representing these compounds we shall make use of the formulas, $\text{HO}:\text{OH}$, $\text{H}_2\text{N}:\text{OH}$ and $\text{H}_2\text{N}:\text{NH}_2$, in which the colons indicate non-polar unions or unions concerning the polarity of which no opinion is expressed. The especial reason for adopting these formulas is that the colon will serve as a label, which will enable us to follow the peroxide oxygen, the hydroxylamine nitrogen and oxygen, and the hydrazine nitrogen in certain reactions we shall discuss later.

Hydrogen peroxide is a powerful augmentor, hydroxylamine is less actively so, while hydrazine only now and then acts as an augmenting agent. Hydrazine may be looked upon as the nitrogen analog of hydrogen peroxide. Hydroxylamine is a mixed compound derived at the same time from water and ammonia.

INTRAMOLECULAR AUGMENTATION OF ALCOHOLS TO ALDEHYDES AND KETONES

The alkyl chloramines

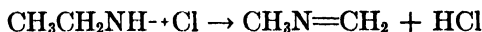
The compounds $\text{RCH}_2\text{NH}^+\text{Cl}$ and $(\text{RCH}_2)_2\text{N}^+\text{Cl}$, containing augmentable alcohol groups and an augmentor in the form of hypochlorous acid chlorine, undergo intramolecular augmentation and reduction reactions which in principle are Hofmann rearrangements.

Ethylchloramine, *ethyl ammonohypochlorite*, $\text{CH}_3\text{CH}_2\text{NH}^+\text{Cl}$. Unfortunately all that is definitely known concerning the decomposition of this compound is that aldehydes, presumably formaldehyde and acetaldehyde, are obtained by warming the chloramine with alcoholic potassium hydroxide and heating the resulting solution with hydrochloric acid (6). However, in view of Berg's discussion of his observations, it is reasonable to say that the decomposition of ethylchloramine takes place partly in accordance with the equation

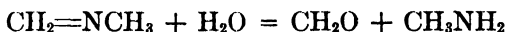


which represents the intramolecular augmentation of an ethyl alcohol group to an acetaldehyde group and the concomitant reduction of hypochlorous acid chlorine to hydrochloric acid chlorine, followed by the hydrolysis of ethylideneimine to aquoacetaldehyde and ammonia.

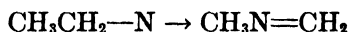
Since methylamine was found among the decomposition products, it may be further assumed that ethylechloramine decomposes in part in accordance with the equation



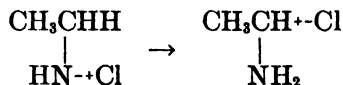
and that the methylmethyleimine thus formed is hydrolyzed to aquoformaldehyde and methylamine



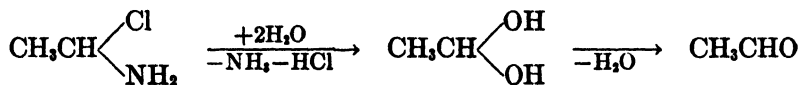
Following Stieglitz (62) these results are to be explained on the assumption that ethylechloramine breaks down directly to form hydrochloric acid and the unstable univalent nitrogen compound, $\text{CH}_3\text{CH}_2\text{—N}$ and that the two-thirds free nitrogen in the ephemeral compound thus formed nitridizes the ethyl alcohol group, $\text{CH}_3\text{CH}_2\cdot$ to the acetaldehyde group, $\text{CH}_3\text{CH}\ddagger$, the univalent nitrogen itself simultaneously undergoing reduction to ammonia nitrogen, with the result that ethylideneimine is formed. At the same time another portion of the ephemeral compound is converted into methylmethyleimine as the result of the augmentation of carbon to carbon union in the ethyl alcohol group.



Quite as legitimately, however, it may be assumed that the first step in the decomposition of ethylechloramine to form acetaldehyde takes place as represented by the equation



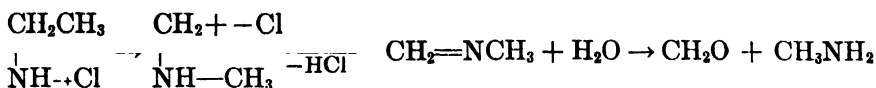
in accordance with which a Beckmann-like rearrangement, involving an exchange of positions of the chlorine atom of the hypochlorous acid group and one of the hydrogen atoms of the CH_2 group, brings about the augmentation of the ethyl alcohol group to an aldehyde group and the concomitant reduction of hypochlorous acid chlorine to hydrochloric acid chlorine. The unknown aldehyde amide-chloride thus formed may either undergo hydrolysis



or it may lose hydrochloric acid directly, thereby passing over into ethyldeneimine, which in turn is hydrolyzed to aquoacetaldehyde and ammonia.



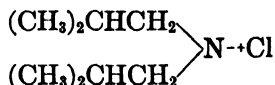
In a similar manner as represented herewith



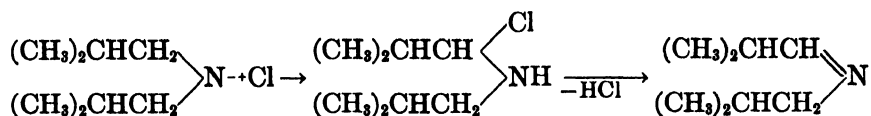
aquoformaldehyde and methylamine are formed. It is to be noted that here it is the methyl group and the chlorine atom which change places, with the result that the carbon to carbon union in the ethyl group is augmented.

It is clear from the preceding discussion that it is scarcely possible to say which of the described mechanisms constitutes the first step in the conversion of ethylchloramine into acetaldehyde. Moreover, for many of the rearrangements to be considered later, similar alternative explanations are possible. We shall find as we proceed that certain rearrangements are simply explained on the assumption of the primary formation of a univalent nitrogen compound, while in others the formation of such compounds is scarcely possible. Finally it will appear that all the Hofmann-Beckmann-Curtius-Lossen rearrangements, without exception, may be explained on the assumption of the primary formation of rearrangement products after the pattern of the conversion of ethylchloramine into acetaldehyde chloride-amide.

Diisobutylchloramine,



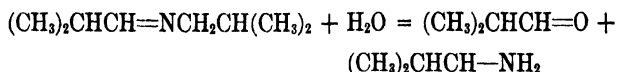
In the presence of a warm alcoholic solution of sodium hydroxide, diisobutyl ammonohypochlorite decomposes to form isobutylisobutylideneimine and hydrochloric acid, say, in accordance with the equation,



The acetal represented by the intermediate formula,⁴ which has not been isolated, loses hydrochloric acid to form isobutylisobutylideneimine. By

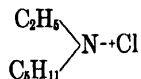
⁴ An isobutyraldehyde amide-chloride in which amido hydrogen is replaced by an isobutyl alcohol group.

the action of dilute hydrochloric acid, Berg (8) hydrolyzed this acetal to aquoisobutyraldehyde and isobutylamine,

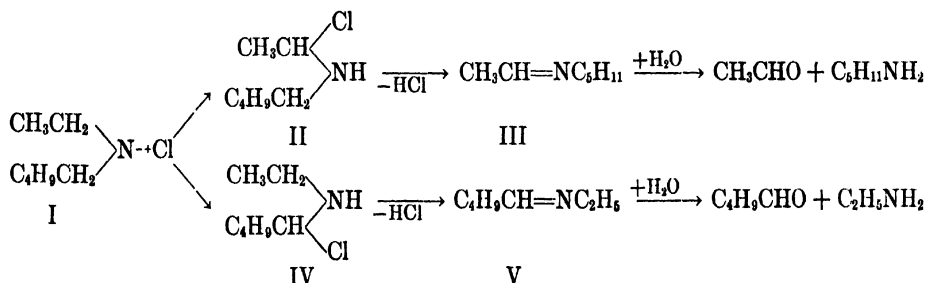


Certainly a univalent nitrogen compound is not formed when diisobutylchloramine loses hydrochloric acid.

Ethylisoamylchloramine,



Berg (9) obtained acetaldehyde, isovaleraldehyde, ethylamine, and isoamylamine by treating ethylisoamylchloramine with alcoholic sodium hydroxide and adding to the reaction mixture an excess of aqueous hydrochloric acid. The manner of formation of these compounds is clear. As summarized by the scheme,

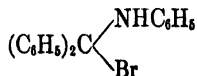


ethylisoamylchloramine rearranges partly to II and partly to IV. These hypothetical compounds readily lose hydrochloric acid to form the aldehyde-acetals III and V, which under the action of aqueous hydrochloric acid are hydrolyzed, the one to aquoacetaldehyde and isoamylamine, the other to isovaleraldehyde and ethylamine.

Triphenylmethylbromamine, $(\text{C}_6\text{H}_5)_3\text{CNH} \cdots \text{Br}$. Miss Vosburgh (64, 70, 75) found that this triphenylmethyl ester of an ammonohypobromous acid when heated with soda lime is decomposed into phenylbenzophenoneimine and hydrobromic acid.

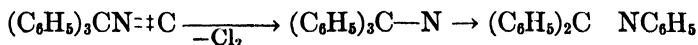


Independent of the question as to whether the formation of a univalent nitrogen compound, $(\text{C}_6\text{H}_5)_3\text{CN}$, or of a mixed ketone-acetal,

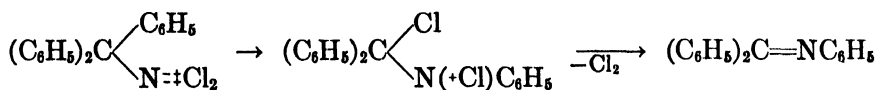


constitutes the initial step in the reaction, it is clear that what Miss Vosburgh accomplished was the augmentation of a tertiary alcohol to a ketone-acetal, using bromine as the primary augmenting agent.

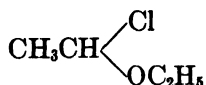
Miss Vosburgh found also that triphenylmethyldichloramine when heated with soda lime yields chlorine and phenylbenzophenoneimine. The reactions involved may be explained as taking place with the intermediate formation of univalent nitrogen,



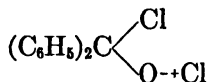
or it may be assumed that one of the hypochlorous acid chlorine atoms augments a paraffin carbon to phenyl carbon union,



following which the positive and negative chlorine are eliminated as elementary chlorine, leaving phenylbenzophenoneimine. The hypothetical intermediate compound is a ketone-acetal which may be compared with the aldehyde-acetal,



known as monochlorodiethyl ether, or better with the unknown acetal of the formula,



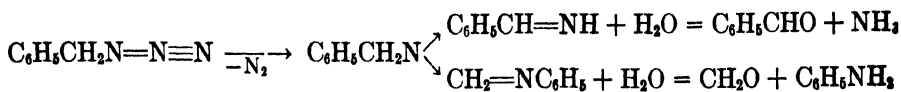
The alkyl azides, esters of ammononitric acid

Since hydrazoic acid is an active nitridizing agent, it is reasonable to expect that the alkyl azides will be found to undergo intramolecular nitridation-reduction reactions closely similar to those involved in the transformations of the chloramines. Little or nothing is known of the manner of decomposition of methyl azide or ethyl azide.

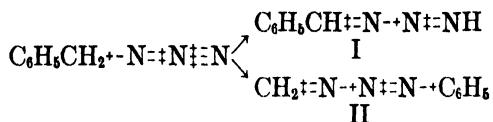
Benzyl azide, benzyl ammononitrate, $\text{C}_6\text{H}_5\text{CH}_2\text{-N} \equiv \text{N} \ddot{\text{N}}$. This azide, which is remarkably stable toward alkalies, gives abundant yields of benzaldehyde, ammonia, formaldehyde, nitrogen, and aniline when heated with dilute sulfuric acid (16, 17).

The reactions involved in the formation of these compounds have been

explained as taking place by way of a univalent nitrogen compound as follows,

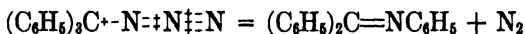


However it may well be that the first step in the decomposition of benzyl azide consists of a Beckmann-like rearrangement,



in accordance with which benzyl ammononitrate, by intramolecular augmentation and reduction, rearranges partly into the benzaldehyde nitrous acid acetal (I) and partly into the formaldehyde acetal (II). Neither of these compounds is known.⁵ Compound I would be expected to lose nitrous anammonide (nitrogen) to form benzylideneimine, which in the presence of water is hydrolyzed to aquobenzaldehyde and ammonia. The second compound, losing nitrogen, would form phenylmethyleimine, $\text{CH}_2\text{NC}_6\text{H}_5$, which readily hydrolyzes to aquoformaldehyde and aniline. Whether in these rearrangements the primary reaction involves the formation of an ephemeral univalent nitrogen compound or the unstable nitrous acid acetals, it does not seem possible in the present state of our knowledge to say. Whatever the details of the reactions concerned may be, it is clear that a benzyl alcohol group is augmented partly to a benzaldehyde group and partly to a formaldehyde group, while at the same time nitric acid nitrogen is reduced to nitrous acid nitrogen.

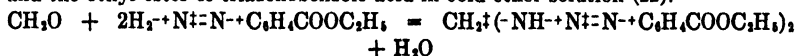
Triphenylmethyl azide, $(\text{C}_6\text{H}_5)_3\text{C--N}::\text{N}::\text{N}$. Senior (60) has shown that triphenylmethyl azide under the action of heat alone gives a good yield of phenylbenzophenoneimine. As represented by the equation,



the reactions involved consist in the augmentation of a tertiary alcohol, in the form of its ammononitric acid ester, to a ketone-ether, and the simultaneous reduction of nitric acid nitrogen to nitrous acid nitrogen.

An intermediate step in the conversion of triphenylmethyl azide into phenylbenzophenoneimine and nitrogen may be the formation of the

⁵ It is interesting to note that an unstable compound closely related to the hypothetical compound (II) above has been obtained by the interaction of formaldehyde and the ethyl ester of triazenobenzoic acid in cold ether solution (22).



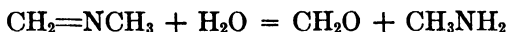
univalent nitrogen compound, $(\text{C}_6\text{H}_5)_3\text{CN}$, or possibly, after the manner indicated above for the decomposition of benzyl azide, of the ketone nitrous acid acetal, $(\text{C}_6\text{H}_5)_2\text{C}^+=\text{N}^-\cdot\text{N}^+=\text{N}^-\cdot\text{C}_6\text{H}_5$.

Alkyl nitramides, esters of aquo-ammononitric acid

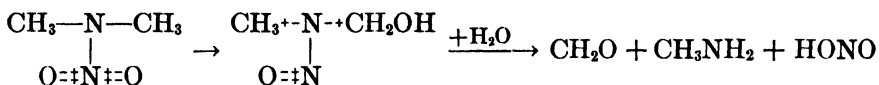
Certain N,N-dialkyl derivatives of nitramide have been found to undergo decomposition in a manner closely resembling that of the azides discussed above. Dimethylnitramide, for example, when warmed with potassium hydroxide yields methylamine, formaldehyde, and nitrous acid (74), perhaps by direct scission into nitrous acid and methylmethylenimine,



followed by the hydrolysis of the formaldehyde-ether to formaldehyde and methylamine,



but more probably in accordance with the scheme,

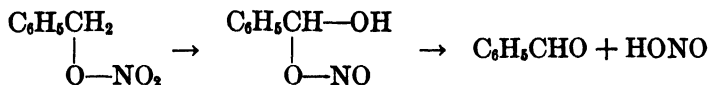


which represents first, the intramolecular oxidation of one of the methyl groups of an ammono methyl alcohol to a formaldehyde group and second, the hydrolysis of the formaldehyde methyl nitrous acid acetal thus formed to aquoformaldehyde, methylamine, and aquonitrous acid.

Alkyl aquonitrates

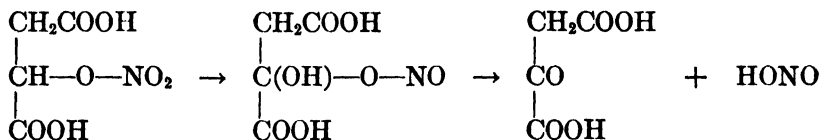
Certain alkyl nitrates appear to undergo intramolecular oxidation and reduction in a similar manner. For example, it has been found that benzyl nitrate decomposes quantitatively into nitrous acid and benzaldehyde when gently heated with alcoholic potassium hydroxide (12, 50).

Nef explains the reaction as consisting in the dissociation of benzyl nitrate into the benzylidene group and nitric acid, followed by the oxidation of the free benzylidene group to benzaldehyde and the reduction of nitric acid to nitrous acid. It would seem more reasonable to say that the reactions take place in accordance with the scheme,



which represents the nitric acid ester as undergoing rearrangement to a nitrous acid half-acetal, followed by the decomposition of this hypothetical compound to form benzaldehyde and nitrous acid (potassium nitrite).

According to Lachman (40) nitromalic acid under the action of potassium hydroxide gives a fair yield of oxalacetic acid,

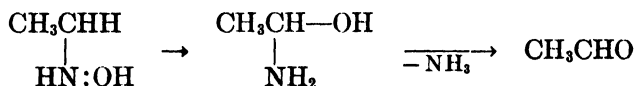


By intramolecular rearrangement the secondary alcohol nitric acid ester part of the nitromalic acid molecule is converted into a ketone nitrous acid acetal, which decomposes to form oxalacetic acid and nitrous acid.

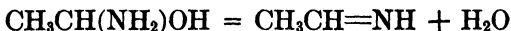
The alkylhydroxylamines

Many derivatives of hydroxylamine undergo intramolecular rearrangements which clearly consist in the augmentation of alcohols to aldehydes or ketones, and since the oxime part of the molecule may act as a purveyor of either oxygen or nitrogen, the resulting aldehydes and ketones may belong either to the oxygen or to the nitrogen system.

N-Ethylhydroxylamine, $\text{C}_2\text{H}_5\text{NH:OH}$. When this compound is heated with dilute hydrochloric acid, acetaldehyde and ammonia are formed (39). The reactions involved may be explained as taking place by way of the univalent nitrogen compound, $\text{CH}_3\text{CH}_2\text{N}$, or in accordance with the scheme,



which represents first the augmentation of an ethyl alcohol group to an acetaldehyde group and the simultaneous reduction of the hydroxylamine group to form aldehyde ammonia, and second, the deammonation of this product of the rearrangement to acetaldehyde.⁶

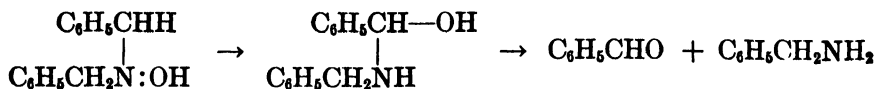


N-Isopropylhydroxylamine, $(\text{CH}_3)_2\text{CH-NH:OH}$. Kjellin found also that acetone and ammonium chloride are formed when *N*-isopropylhydroxylamine hydrochloride is heated in the dry state. After the manner of the conversion of a primary alcohol hydroxylamine into an aldehyde and ammonia as explained above, so here a secondary alcohol oxime rearranges to form a ketone and ammonia.

⁶ It is interesting in this connection to recall that aldehyde ammonia is deammonated to acetaldehyde in the presence of acids in water solution as represented by the above equation and that in liquid ammonia solution in the presence of calcium amide it is dehydrated to ethylideneimine.

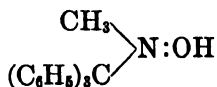


N,N-Dibenzylhydroxylamine, $(\text{C}_6\text{H}_5\text{CH}_2)_2\text{N}:\text{OH}$. When this primary alcohol derivative of hydroxylamine is heated with acetic acid saturated with hydrochloric acid gas, it is converted practically quantitatively into benzaldehyde and benzylamine (76). It may be assumed that the reactions involved take the course

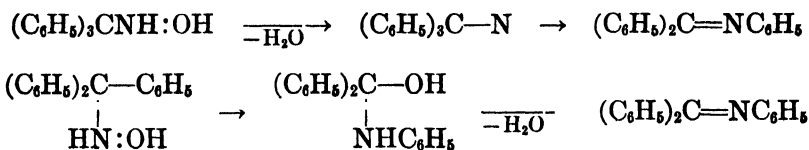


The first step consists in a Beckmann-like rearrangement of dibenzylhydroxylamine to form a benzaldehyde-acetal; the second in the breaking down of this acetal to form an aldehyde and an alcohol after the familiar manner of acetals in the presence of mineral acids.

N-Triphenylmethylhydroxylamine, $(\text{C}_6\text{H}_5)_3\text{C}-\text{NH}:\text{OH}$ and *N*-triphenylmethyl-*N*-methylhydroxylamine,



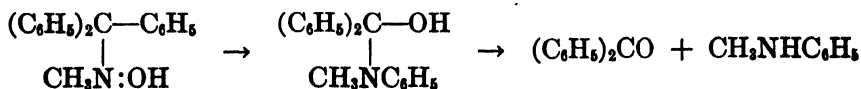
When the first compound, in ether solution, is treated with phosphorus pentachloride, a practically quantitative yield of phenylbenzophenone is obtained (68). Whether the reactions involved take place in accordance with the one or the other of the schemes,



it is difficult to say. In any event a tertiary alcohol undergoes augmentation to form a ketone-ether, hydroxylamine simultaneously undergoing reduction to ammonia and water.

Under similar treatment the second compound gives moderate yields of methylaniline and benzophenone (69).

While the decomposition of the first compound has been represented as following either of the familiar routes as indicated above, it is not so easy to explain the decomposition of the second compound on the assumption of the formation of an intermediate compound containing univalent nitrogen (68, 69). The reactions may, however, be represented as follows:

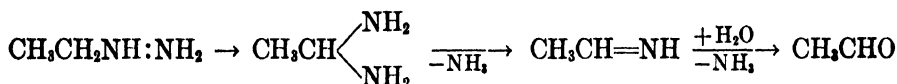


N-triphenylmethyl-*N*-methylhydroxylamine undergoes in effect a Beckmann rearrangement to form a ketone-acetal, which decomposes to form an aquo ketone and an ammonio alcohol.

Triphenylmethylmethylchloramine, $(\text{C}_6\text{H}_5)_3\text{C}-\text{NCl}-\text{CH}_3$, according to Miss Vosburgh (65) does not undergo rearrangement.

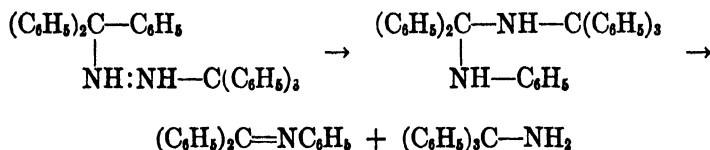
Alkylhydrazines

Since hydrazine may be looked upon as a nitrogen analog of hydrogen peroxide, it is reasonable to assume that it possesses nitridizing properties, and that in particular certain of its derivatives will be found to undergo intramolecular reactions similar to those which have been shown to characterize the alkyl derivatives of hydroxylamine and the esters of the ammonohypochlorous acids and of hydrazoic acid. For example, ethylhydrazine might be expected to undergo intramolecular nitridation and reduction as represented by the scheme,



to form aquoacetaldehyde and ammonia. As a matter of fact, however, none of the simpler alkyl derivatives of hydrazine has been observed to undergo such reactions, and this presumably for the reason that hydrazine behaves generally as a powerful reducing agent and only now and then as an augmenting agent.

Symmetrical bis-triphenylmethylhydrazine, $(\text{C}_6\text{H}_5)_3\text{C}-\text{NH}-\text{NH}-\text{C}(\text{C}_6\text{H}_5)_3$. However, Stieglitz and Brown (67) have shown that one of the reactions taking place when symmetrical bis-triphenylmethylhydrazine is heated with zinc chloride results in the formation of phenylbenzophenone-imine and triphenylmethylamine. The reactions, whether involving the formation of a univalent nitrogen compound, $(\text{C}_6\text{H}_5)_3\text{CN}$, or following the course,



consist in the intramolecular nitridation of a tertiary alcohol to a ketone-acetal and the simultaneous reduction of hydrazine nitrogen to ammonia nitrogen.

It is interesting furthermore to recall that Stieglitz and Brown found that bis-triphenylmethylhydrazine at its melting point decomposes practically

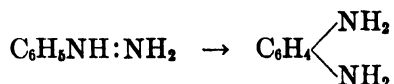
quantitatively into triphenylmethane and nitrogen. This observation is in harmony with experience to the effect that hydrazine and its derivatives generally act as powerful reducing agents. The equation



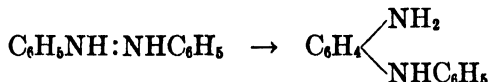
represents the reduction of the tertiary alcohol groups, $(\text{C}_6\text{H}_5)_3\text{C}^+$, to a hydrocarbon, $(\text{C}_6\text{H}_5)_3\text{CH}$, and the augmentation (dehydrogenation) of hydrazine to elementary nitrogen.

Aryl hydrazides

The well-known rearrangements of phenylhydrazine to *p*-phenylenediamine,



and of hydrazobenzene to *p*-semidine,

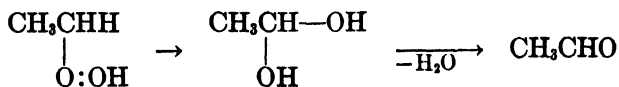


involve the nitridation of a phenyl group to a phenylene group and the reduction of hydrazine nitrogen to ammonia nitrogen. When hydrazobenzene is converted into benzidine, the hydrazine group may be said to nitridize the two phenyl groups to form a diphenyl group, the hydrazine nitrogen at the same time undergoing reduction to ammonia nitrogen.

Alkyl derivatives of hydrogen peroxide

Recalling again the many similarities in the behavior of hydrogen peroxide, hydrazine, and hydroxylamine, it is interesting to find that certain alkyl hydroperoxides have been observed to undergo rearrangements which are clearly analogous to the intramolecular augmentation-reduction reactions discussed above.

Ethyl hydroperoxide, $\text{C}_2\text{H}_5\text{O}:\text{OH}$. Concerning rearrangements of this compound it is known only that in the presence of molecular silver it gives small yields of acetaldehyde and acetic acid (1a). The acetaldehyde is probably formed in accordance with the equation,

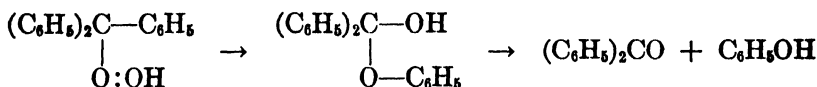


which represents a reaction analogous to that involved in the conversion of ethylhydroxylamine into acetaldehyde and ammonia (p. 230) and of

bis-triphenylmethylhydrazine into phenylbenzophenoneimine and triphenylmethylamine (p. 232).

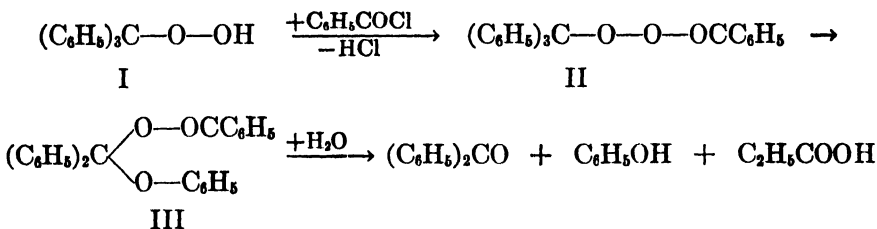
Since the formation of acetaldehyde from ethylhydroxylamine and from ethyl hydroperoxide almost certainly involve similar reactions, it follows that the formation of a univalent nitrogen compound as the first step in the rearrangement of ethylhydroxylamine is highly improbable.

Triphenylmethyl hydroperoxide, $(\text{C}_6\text{H}_5)_3\text{CO}:\text{OH}$, when heated above its melting point decomposes to form benzophenone and phenol (78). While it may be that the compound breaks down directly, it seems more reasonable to assume that a rearrangement takes place and that the resulting ketone-acetal decomposes to form benzophenone and phenol

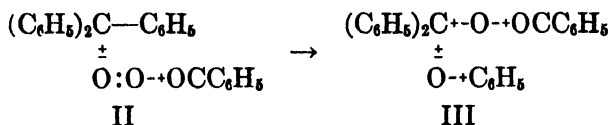


When triphenylmethyl hydroperoxide together with benzoyl chloride is treated with a strong solution of potassium hydroxide a benzophenone-acetal of the formula III below is formed, which under the action of hot alcoholic potassium hydroxide is hydrolyzed to benzophenone, phenol, and benzoic acid.

According to Wieland and Maier the reactions involved take place as follows:



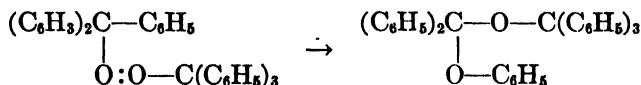
The nature of the transformation of II into III may perhaps be made clearer by writing the equation,



and noting that the exchange of positions of the phenyl and $\text{C}_6\text{H}_5\text{COO}$ groups, in principle a Beckmann rearrangement, involves the augmentation of a tertiary alcohol group to a ketone group and the simultaneous reduction of hydrogen peroxide oxygen. Compound III is a ketone-acetal which should of course readily hydrolyze to benzophenone, phenol, and benzoic acid.

The isolation and identification of the intermediate ketone-acetal (III) in the conversion of triphenylmethyl hydroperoxide into benzophenone and phenol, lends substantial support to our earlier assumptions that similar intermediate compounds are formed in the analogous transformations of the derivatives of chloramine, hydrazoic acid, hydroxylamine, and hydrazine.

Bis-triphenylmethyl peroxide, $(\text{C}_6\text{H}_5)_3\text{C}^+-\text{O}-\text{O}-\text{C}^+(\text{C}_6\text{H}_5)_3$. When this compound is heated with xylene in an atmosphere of carbon dioxide, limited amounts of benzophenone, phenol, and triphenylcarbinol are formed (77). The appearance of these compounds among the reaction products is reasonably accounted for on the assumption that a portion of the bis-triphenylmethyl peroxide undergoes rearrangement,



to form a ketone-acetal which should in turn be hydrolyzable to benzophenone, phenol, and triphenylcarbinol. However, if this explanation of the formation of these compounds is to hold it is necessary to assume that small quantities of water were adventitiously present in Wieland's reaction mixtures. Much the greater portion (75 per cent) of the peroxide undergoes a benzidine-like transformation to form a diethyl ester of benzpinacone with which we do not concern ourselves here.

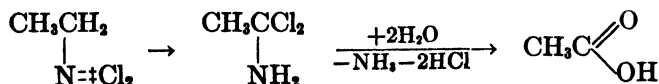
INTRAMOLECULAR AUGMENTATION OF ALCOHOLS TO CARBYLIC ACIDS

Alkyldichloramines

It will be recalled that the alkyl monochloramines yield aldehydes and hydrochloric acid as decomposition products, the one atom of hypochlorous acid chlorine contained in the molecule of the chloramine just sufficing to augment an alcohol group to an aldehyde group. The two hypochlorous chlorine atoms contained in the molecule of the dichloramines may be expected to augment the alkyl groups to carbylic acid groups, $\text{RCH}_2\cdot \rightarrow \text{RC}\ddagger$.

Methyldichloramine, $\text{CH}_3\text{N}=\ddagger\text{Cl}_2$. When heated, methyldichloramine decomposes into hydrocyanic acid (formic anammonide) and hydrochloric acid (5).

Ethyldichloramine, $\text{CH}_3\text{CH}_2\text{N}=\ddagger\text{Cl}_2$. The formation of acetic acid by the action of potassium hydroxide on this ester of an ammonohypochlorous acid as observed by Berg (7) may be represented as taking the course



in accordance with which an acetic acid amide-chloride is primarily formed to decompose in the presence of potassium hydroxide to form aquo-acetic acid.

Isoamylidichloramine, $C_5H_{11}N=+Cl_2$. Berg found also that isoamylidichloramine, when heated with potassium hydroxide, yields isovaleronitrile or isovaleric acid, depending upon the conditions under which the decomposition is effected. It is to be taken as a matter of course that the reactions involved are similar to those discussed above.

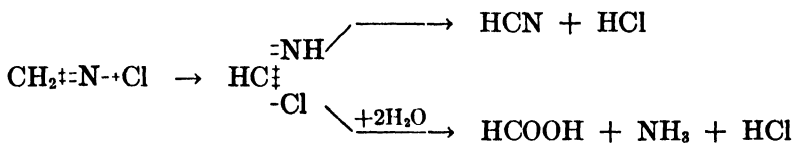
INTRAMOLECULAR AUGMENTATION OF ALDEHYDES AND KETONES TO CARBYLIC ACIDS

The same sort of intramolecular reactions as those which have been discussed above as consisting in the augmentation of alcohols to aldehydes and ketones and of alcohols to carbylic acids or nitriles are also involved in the rearrangement of certain aldehyde and ketone derivatives of monochloramine, hydrazoic acid, and hydroxylamine to carbylic acids.

Alkylidenechlorimines

Methylenechlorimine, $CH_2=N^+-Cl$. By the action of chloramine on formaldehyde in water solution, Cross, Bevan, and Bacon (15) obtained a compound which they believed to be a dimer of methylenechlorimine, $(CH_2=N^+-Cl)_2$. This unstable compound when warmed yields hydrocyanic acid and hydrochloric acid as the main products of decomposition.

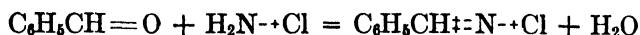
Delépine (19) has shown that by the action of hypochlorous acid on hexamethylenetetramine a trimer of methylenechlorimine, $(CH_2=N^+-Cl)_3$, is formed which on treatment with sodium ethylate gives abundant yields of formic acid and ammonia. The decomposition of the dimer of methylenechlorimine into hydrocyanic acid and hydrochloric acid and the action of sodium ethylate on the trimer to form formic acid and ammonia may be explained as follows. Writing the monomolecular formula for methylenechlorimine, the scheme



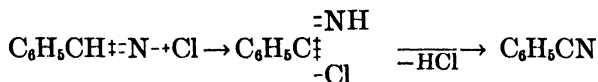
represents: first, the rearrangement of the chlorimine to formic acid imide-chloride after the manner of a Beckmann rearrangement; second, the decomposition of this unknown acid imide-chloride to form hydrocyanic acid and hydrochloric acid; and third, its hydrolysis to formic acid, ammonia, and hydrochloric acid.

Benzylidenechlorimine, $C_6H_5CH=N^+-Cl$. Raschig (54) obtained this

benzaldehyde hypochlorous acid acetal in the form of an unstable yellow oil mixed with more or less benzaldehyde, by shaking a water solution of chloramine with benzaldehyde.



When this oil was warmed with sodium hydroxide solution, or even with water, phenyl cyanide was formed. Clearly the decomposition of benzyldenechlorimine into benzonitrile and hydrochloric acid may be said to consist, in principle, in the augmentation of an aldehyde to a carbylic acid and the reduction of hypochlorous acid to hydrochloric acid,

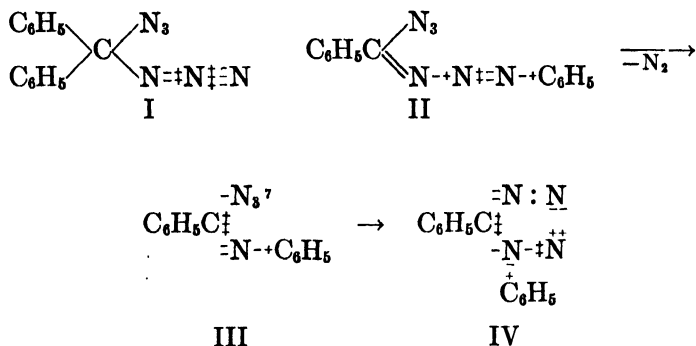


It is important to note in this connection that attempts to effect the rearrangement of benzophenonechlorimine have failed (66).

Ketone azides

No aldehyde azides appear to be known. However, at least two ketone azides have been observed to undergo intramolecular reactions which resemble the Beckmann rearrangement of the ketoximes.

Benzophenone diazide, $(\text{C}_6\text{H}_5)_2\text{C}(\text{N}=\text{N}^+\equiv\text{N})_2$. Schroeter (56) has shown that this ketone nitric acid acetal is converted into 1,5-diphenyltetrazole when heated in an indifferent solvent. It is reasonable to suppose that the reactions involved follow the course,



The ketone diazide (I) undergoes intramolecular nitridation of the diphenylketone group to a benzoic acid group and reduction of nitric acid nitrogen to nitrous acid nitrogen to form the hypothetical compound II,⁷

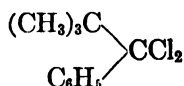
⁷ The azide group is here assumed to act as a nitrous acid hydrazide (cf. p. 222.)

⁸ Compare the rearrangement of benzyl azide (p. 227) and of triphenylmethyl hydroperoxide (p. 234).

which, splitting off nitrogen (nitrous anammonide), yields III. Finally, after the manner of the intramolecular ammonation of guanyl azide to 5-aminotetrazole the azide (III) is transformed into 1,5-diphenyltetrazole (IV).⁹

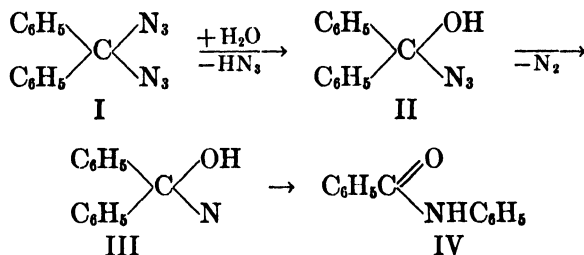
Independently of whether the primary reaction consists in the formation of an univalent nitrogen compound, as was assumed by Schroeter, or of rearrangement to the benzoic acid nitrous acid derivative (II), what happens first and last is that by the nitridizing action of nitric acid nitrogen a diphenyl ketone is converted into a derivative of benzoic acid.

Just as benzophenone diazide is converted into 1,5-diphenyltetrazole, as explained above, so in a similar manner 1-tertiary-butyl-5-phenyltetrazole is formed when pivalophenone dichloride,

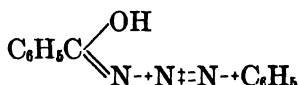


is heated with silver azide in amyl ether solution (58).

Götzky (30), who has recently isolated benzophenone diazide, has shown that quantitative yields of benzanilide are obtained when benzophenone diazide is treated with cold 70 per cent sulfuric acid. According to Götzky the reactions follow the course,



Quite as reasonably it may be assumed that compound II, instead of losing nitrogen directly to form III, rearranges into



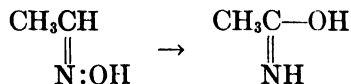
which by the elimination of a molecule of nitrogen (nitrous anammonide) passes over into benzanilide (IV). Whatever course the reactions involved may follow, it is clear that first and last a ketone is augmented to a carboxylic acid.

⁹ 1,5-Diphenyltetrazole is a cyclic benzoic acid nitrous acid hydrazide, and at the same time a phenyl ester of a mixed benzoic nitrous acid.

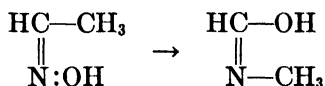
Aldoximes and ketoximes

The aldoximes and ketoximes in general under the influence of certain reagents undergo the familiar Beckmann rearrangement to acid amides. Acetaldoxime, for example, on treatment with phosphorus pentachloride is converted into a mixture of acetamide and methylformamide (23).

Representing the formation of acetamide by the equation,

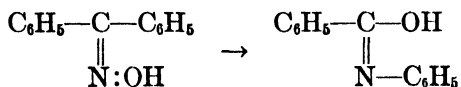


and of methylformamide by



it may be said that by processes of intramolecular augmentation and reduction, acetaldehyde is converted partly into an aquo-ammonoacetic acid and partly into an *N*-methyl ester of an aquo-ammonoformic acid. Whatever the detailed mechanism of the Beckmann rearrangement may be, it is here represented as consisting simply in an exchange of positions on the part of aldehyde hydrogen and the OH of the oxime group in the one case and of the methyl group and the OH group on the other. In both cases aldehyde carbon is augmented to carbylic acid carbon, while the hydroxylamine residue is at the same time, in effect, reduced to ammonia and water.

In a similar manner the ketoximes undergo rearrangement to carboxylic acid esters; benzophenoneoxime, for example, to benzanilide,



O-Methylbenzophenoneoxime does not undergo the Beckmann rearrangement. When heated with acids it is hydrolyzed to benzophenone and *O*-methylhydroxylamine (1).

Hydrazones

In view of the many similarities in the behavior of hydroxylamine and hydrazine, it might be expected that hydrazones would be found to undergo rearrangements in accordance with the equation, $\text{RCH}=\text{N}:\text{NH}_2 \rightarrow \text{RC}(\text{NH})\text{NH}_2$, which represents an hypothetical transformation whereby an aldehyde hydrazone, undergoing intramolecular augmentation and reduction, is converted into a carbazylic acid.

Apparently none of the aldehyde and ketone derivatives of hydrazine

or of phenylhydrazine have been observed to undergo the rearrangements. Instead, with loss of ammonia, certain phenylhydrazones are converted into derivatives of indole (11, 25).

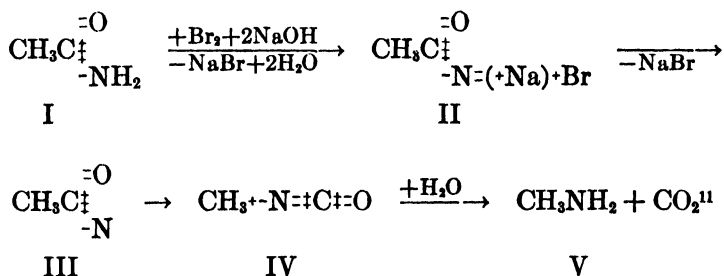
INTRAMOLECULAR AUGMENTATION OF CARBYLIC ACIDS TO CARBONIC ACIDS

The reactions involved in the conversion of acetbromamide into methyl isocyanate and hydrobromic acid, of benzoyl azide into phenyl isocyanate and nitrogen, of benzo-hydroxamic acid into phenyl isocyanate and water, and of benzamidoxime into phenylurea may be looked upon as consisting in the intramolecular augmentation of carbylic acids to carbonic acids, and the reduction, respectively, of hypobromous acid bromine to hydrobromic acid bromine, of nitric acid nitrogen to nitrous acid nitrogen, and of hydroxylamine nitrogen and oxygen to ammonia nitrogen and water oxygen.

Acyl halogen amides

These compounds are formed by the action of alkali hypohalites on acid amides and in turn are converted into primary amines and alkali carbonates by the action of hot alkali solution.

Acetbromamide, $\text{CH}_3\text{CO}-\text{NH}\cdot+\text{Br}$. The reactions concerned in the well-known process of Hofmann (35, 72) for the preparation of methylamine from acetamide have been explained as following the steps represented by the scheme,¹⁰



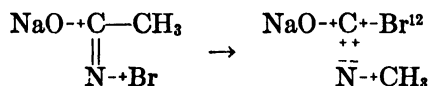
Under the action of bromine and sodium hydroxide an aquo-ammonoacetic acid (I) is converted into the sodium salt of a mixed aquo-ammonoacetic ammonohypobromous acid (II). This salt, losing sodium bromide,

¹⁰ Excepting that the small plus and minus signs are used in the sense already explained (p. 221).

¹¹ No one of the formulas, CH_3CONHBr , $\text{CH}_3\text{C(OH)Br}$ or $\text{CH}_3\text{C(NH)OBr}$, has been established as representing the constitution of acetbromamide. According to Hantzsch (34) the sodium salt of acetbromamide has the constitution represented by the formula, $\text{CH}_3\text{C(NH)ONa}$. Whether the metal is attached to oxygen or nitrogen, or neither, is a question which need not concern us here.

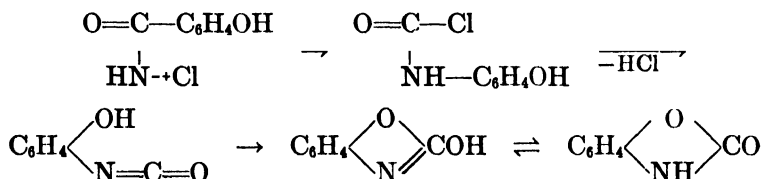
forms the univalent nitrogen compound III. The *N*-methyl aquo-ammonocarbonate (IV) formed by the rearrangement of III is hydrolyzed by the action of sodium hydroxide to sodium carbonate and the ammono alcohol V.

Quite as reasonably it may be assumed that the hypobromite bromine contained in the sodium salt of acetbromamide augments the carbon to carbon bond by simply changing places with the methyl group

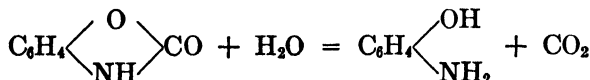


thereby bringing about a Beckmann-like rearrangement; and that the compound thus formed, which is at the same time a bromide, a sodium salt, and an *N*-methyl ester of a carbonic acid, loses sodium bromide to yield methyl isocyanate.¹³

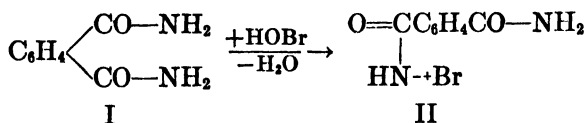
An example of the conversion of a carboxazylic acid into a cyclic aquo-ammonocarbonic acid is the formation of oxycarbanil by the action of sodium hypochlorite in alkali solution on salicylamide (31) as represented by the scheme



A silver salt, $\text{C}_7\text{H}_4\text{O}_2\text{NAg}$, and several *N*-esters and *O*-esters of this cyclic phenylene aquo-ammonocarbonate have been prepared. Oxycarbanil has been hydrolyzed to *o*-aminophenol and carbon dioxide.

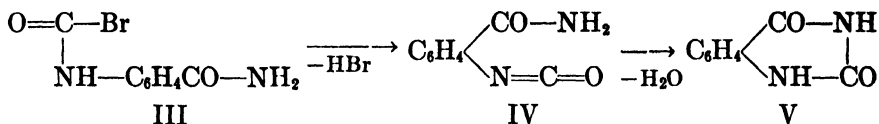


A third example of the Hofmann transformation is the formation of benzoyleneurea by the action of potassium hypobromite on phthalamid (37). The reactions involved may be represented by the scheme,



¹² Mohr (47) has shown that almost certainly an *N*-phenylcarbamate, $\text{C}_6\text{H}_5\text{NH}-\text{CO}-\text{OK}$, is formed as an intermediate product when benzchloramide undergoes rearrangement under the action of aqueous potassium hydroxide.

¹³ Hoogewerff and van Dorp (36) first suggested that this unknown carbonic acid derivative is the primary product of the rearrangement of bromoacetamide.



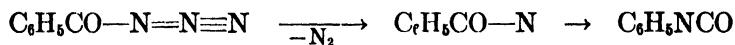
and explained as consisting: first, in the conversion of a carboxylic acid group into a carboxylic acid ammonohypobromous acid group under the action of potassium aquohypobromite (I to II); second, in the intramolecular augmentation (nitridation) of a carbylic acid carbon to a phenylene carbon union and the simultaneous reduction of hypobromous bromine to hydrobromic acid bromine (II to III); third, in the loss of hydrobromic acid from this carbonic acid ester bromide to give the aquo-ammonocarbonic derivative (IV); and finally, in the intramolecular ammonation of this compound to form the cyclic benzoic acid carbonic acid ester (V).

In support of his hypothesis that the primary step involved in the Hofmann rearrangement is the formation of a univalent nitrogen compound, Stieglitz (63) calls attention to the fact that neither the *N*-alkyl (aryl) derivatives of the acyl halogen amides, $\text{RCON}(\text{Hl})\text{R}'$, nor their isomers, the *N*-halogen acyl imino esters, $\text{RC}(\text{NHl})\text{OR}'$, undergo this rearrangement (38, 61).

Acyl azides

In some cases when heated alone and in general when heated in an indifferent solvent, the acid azides decompose into nitrogen and isocyanates.

Benzoyl azide, $\text{C}_6\text{H}_5\text{CO}-\text{N}=\text{N}^+\text{N}^-\text{N}$. Schroeter (18, 57) has shown that benzoyl azide decomposes quantitatively to form phenyl isocyanate and nitrogen when heated in the presence of dry benzene. While the decomposition is generally assumed to follow the course

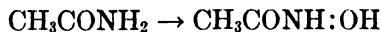


by way of an univalent nitrogen compound, it may be that the acid azide, by intramolecular nitridation and reduction, first rearranges to a nitrous acid carbonic acid derivative of the formula, $\text{C}_6\text{H}_5^+-\text{N}=\text{N}^+-\text{N}=\text{C}^+=\text{O}$,¹⁴ which unknown compound should break down to form phenyl isocyanate and nitrogen. Clearly a benzoic acid derivative is augmented to an *N*-phenyl ester of an aquo-ammonocarbonic acid, while at the same time ammononitric acid undergoes reduction to a nitrous acid which appears in the form of its anammonide, namely as free nitrogen.

¹⁴ Two nearly related compounds of the formulas, $\text{C}_6\text{H}_5^+-\text{NH}^+-\text{CO}^+-\text{NH}^+-\text{N}^+=\text{N}^+-\text{C}_6\text{H}_4\text{COOH}$ and $\text{C}_6\text{H}_5^+-\text{NH}^+-\text{CO}^+-\text{NH}^+-\text{N}^+=\text{N}^+-\text{C}_6\text{H}_4\text{COOC}_2\text{H}_5$, which are derivatives of an hypothetical nitrous carbonic acid, $\text{H}_2\text{N}^+-\text{CO}^+-\text{NH}^+-\text{N}^+=\text{NH}$, have been prepared (21).

Hydroxamic acids

Just as one may look upon acetbromamide as an aquo-ammonoacetic acid the amide group of which is "bromidized" to an ammonohypobromous acid group, and upon benzoyl azide as an aquo-ammonobenzoic acid whose amido group is nitridized to an ammononitric acid group, so similarly acethydroxamic acid may be said to be an aquo-ammonoacetic acid in which the amido group is oxidized to the oxime group.

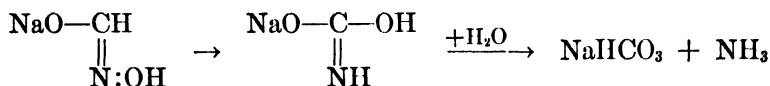


Many hydroxamic acids undergo intramolecular reactions which resemble closely those involved in the Hofmann-Beckmann-Curtius transformations discussed above. Following are examples of the many known Lossen rearrangements.

Formohydroxamic acid,

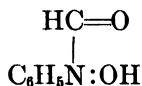


Excepting that the formation of sodium carbonate and ammonia by the slow decomposition of the sodium salt of formohydroxamic acid (10) may be interpreted as taking place in accordance with the scheme,

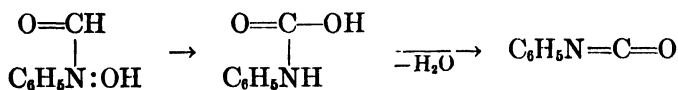


none of the aliphatic hydroxamic acids has been observed to undergo the Lossen rearrangement.

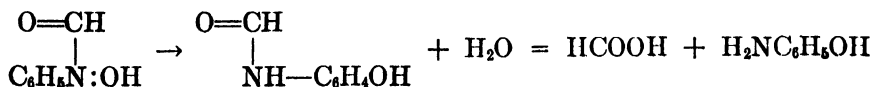
Formylphenylhydroxylamine,



When heated with phosphorus pentoxide formylphenylhydroxylamine undergoes the Lossen rearrangement to form phenyl isocyanate (4). The yield is small.

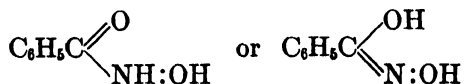


Under the action of boiling normal sulfuric acid the oxime yields formic acid and *p*-aminophenol (2).



In the one case formic acid carbon is augmented to carbonic acid carbon; in the other a phenyl group is augmented to a phenylene group.

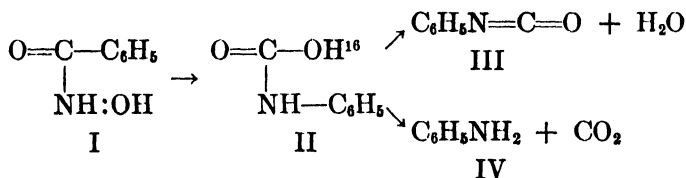
Benzohydroxamic acid,



Aniline, carbon dioxide, phenyl isocyanate, and benzoic acid have been identified among the products of the destructive distillation of benzohydroxamic acid (33, 42).

By the action of thionyl chloride on benzohydroxamic acid in the presence of boiling benzene, phenyl isocyanate is formed (45).

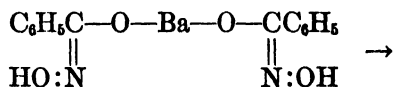
The formation of these compounds, excepting benzoic acid,¹⁵ may be explained as taking place either by way of the univalent nitrogen compound, $\text{C}_6\text{H}_5\text{CO}-\text{N}$, or in accordance with the equation,



which represents the benzoic acid oxime (I) as undergoing rearrangement to form an *N*-phenyl aquo-ammonocarbonate (II), which may on the one hand lose water to form the phenyl aquo-ammonocarbonate (III)¹⁷ and on the other break down to form carbon dioxide and aniline (IV).

When the barium salt of benzohydroxamic acid is strongly heated, two molecules of aniline and one each of barium carbonate and carbon dioxide are obtained from each molecule of the salt, $(\text{C}_6\text{H}_5\text{CO}-\text{NH:O})_2\text{Ba} \cdot \text{H}_2\text{O}$, used (43).¹⁸

As represented by the scheme

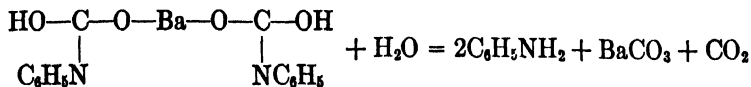


¹⁵ The presence of benzoic acid is to be accounted for on the supposition that water set free in the dehydration of II to III hydrolyzes benzohydroxamic acid to aquobenzoic acid and hydroxylamine. Benzohydroxamic acid is known to undergo this hydrolytic decomposition.

¹⁶ Mohr (48) has shown that phenylcarbamates are formed as intermediate products in the Hofmann rearrangement of benzochloramide.

¹⁷ Phenylcarbamic acid is apparently not known to decompose in this manner.

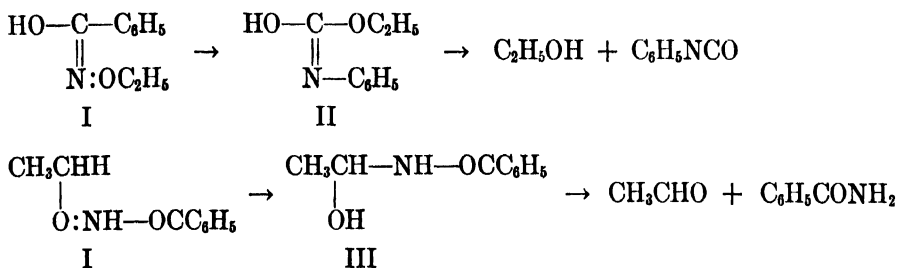
¹⁸ Lossen (41) prepared this salt and reported it as containing no water of crystallization. As a matter of fact the barium content found by Lossen agrees almost exactly with the formula given above for the monohydrated salt.



barium benzohydroxamate rearranges to the barium salt of a phenyl-carbamic acid; this latter compound is then hydrolyzed, by the water of crystallization present in the original salt, to aniline, barium aquocarbonate, and carbon dioxide.

N-Benzoyl-O-ethylhydroxylamine, $\text{C}_6\text{H}_5\text{CO}-\text{NH}:\text{O}-\text{C}_2\text{H}_5$. When heated at 190°C . this compound yields phenyl isocyanate, ethyl alcohol, acetaldehyde, and benzamide (32).

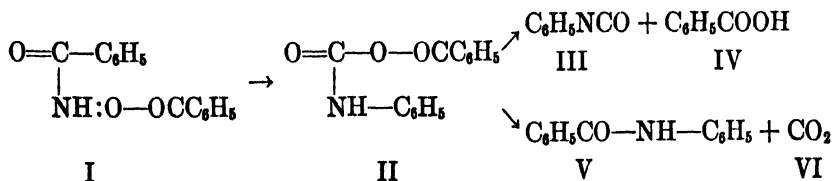
The formation of these products may be explained on the assumption that benzoylethylhydroxylamine rearranges in two ways as follows:



the one rearrangement resulting in the formation of an *O*-ethyl-*N*-phenyl aquo-ammonocarbonate (II) (phenylurethan) which is known to lose alcohol to form phenyl isocyanate, the other in the formation of an unknown *N*-benzoyl acetaldehyde ammonia (III) which should easily decompose to form acetaldehyde and benzamide. Recalling our manner of speaking in earlier connections, it may be said that on the one hand benzoic acid is augmented to an aquo-ammonocarbonic acid (I to II), and that on the other hand ethyl alcohol is augmented to acetaldehyde (I to III), the augmenting agent, hydroxylamine, at the same time undergoing reduction to ammonia and water.

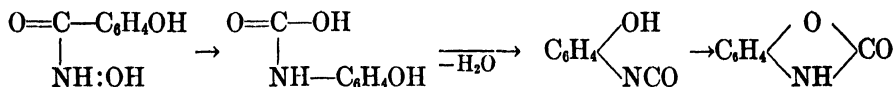
N,O-dibenzoylhydroxylamine, $\text{C}_6\text{H}_5\text{CO}-\text{NH}:\text{O}-\text{OCC}_6\text{H}_5$. When this compound is heated it decomposes almost quantitatively to form phenyl isocyanate, benzoic acid, benzanilide, and carbon dioxide (20, 52).

It may be assumed that the reactions involved take place as represented by the scheme,



in accordance with which an *N*-phenyl ester of a benzoylcarbonic acid, resulting from the Lossen rearrangement of I to II, breaks down partly to form the aquo-ammonocarbonic acid ester (III) and aquobenzoic acid (IV), and partly to the phenyl aquo-ammonobenzoate (V) and carbonic anhydride.

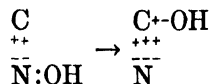
Salicylhydroxamic acid, $\text{HO}-\text{C}_6\text{H}_4\text{CO}-\text{NH}:\text{OH}$. Under the influence of thionyl chloride in the presence of boiling benzene, salicylhydroxamic acid is converted into oxycarbanil (46, 59). As represented by the scheme,



salicylhydroxamic acid undergoes the Lossen rearrangement to form a cyclic *o*-phenylene aquo-ammonocarbonate (cf. p. 241).

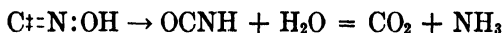
Fulminic acid, carbonous acid oxime, $\text{C}\equiv\text{N}:\text{OH}$. A clean-cut rearrangement of fulminic acid to cyanic acid or of a metallic fulminate to a metallic cyanate has apparently never been accomplished. None the less, observations are on record which show that this carbonous acid oxime undergoes rearrangement in a manner identical in principle with the Lossen transformation of the hydroxamic acids.

Schischkow (55) found many years ago that "isocyanic acid" appears among the products formed by the action of boiling aqueous solutions of alkali halides on mercuric fulminate and that potassium cyanate—or rather its hydrolytic products, potassium carbonate and ammonia—are formed in considerable yields when mercuric fulminate is exposed to the action of boiling potassium hydroxide solution. The reactions involved may be interpreted as constituting a Lossen rearrangement



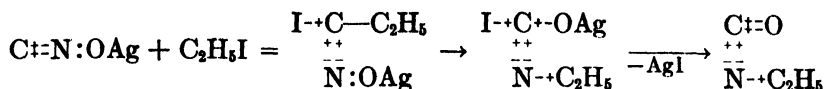
in accordance with which carbonous acid carbon is augmented to carbonic acid carbon, while at the same time hydroxylamine is reduced, in principle, to ammonia and water.

When mercuric fulminate is heated with dilute sulfuric acid carbon dioxide, ammonia, hydroxylamine, and mercurous sulfate are formed (13). Carbon dioxide and ammonia, it may be assumed, result from a Lossen rearrangement of fulminic acid.



Nef (49) has shown that ethyl isocyanate, in the monomolecular and trimolecular states, is formed when ethyl iodide in ether solution is allowed

to stand in contact with silver fulminate. Whatever the course of the reactions involved may be, say, as a reasonable surmise in accordance with the scheme,

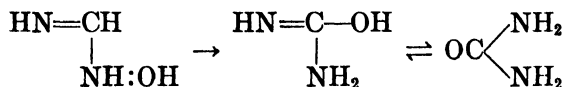


it is clear that a carbonous acid oxime undergoes a Lossen rearrangement to form an aquo-ammonocarbonic acid ester.

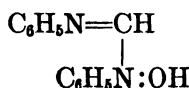
Amidoximes

Like the hydroxamic acids, the amidoximes are carbylic acid oximes, and as such should be found to undergo intramolecular augmentation and reduction reactions similar to those discussed above.

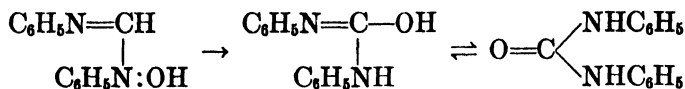
Formamidoxime, $\text{HC}(\text{NH})\text{NH:OH}$, $\text{HC}(\text{NH}_2)\text{N:OH}$, does not undergo clean-cut rearrangement. However, the presence of urea among the products formed by heating formamidoxime in water solution may be explained on the assumption that a Lossen rearrangement takes place (44).



N-Phenylimidoformyl-N-phenylhydroxylamine,



It has been found that this diphenyl derivative of formamidoxime gives a nearly quantitative yield of *N,N'*-diphenylurea when treated with acetic anhydride (3). The reactions involved as represented by the scheme,

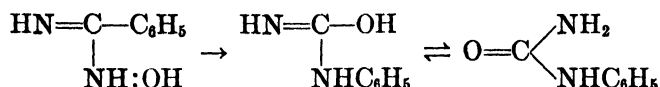


may be said to consist in the intramolecular augmentation of a derivative of formic acid to a diphenyl aquo-ammonocarbonate with an hydroxylamine group functioning as augmenting agent.

Under the action of hot dilute sulfuric acid *N*-phenylimidoformyl-*N*-phenylhydroxylamine yields formic acid, aniline, and *p*-aminophenol instead of undergoing the Lossen rearrangement.

Benzamidoxime, $\text{C}_6\text{H}_5\text{C}(\text{NH})\text{NH:OH} \rightleftharpoons \text{C}_6\text{H}_5\text{C}(\text{NH}_2)\text{N:OH}$. Neither when heated alone nor with acids or alkalis does this acid oxime undergo rearrangement. However Pinnow (53, 73) found that *N*-phenylurea is formed when a suspension, in chloroform, of an intimate mixture

of benzamidoxime and sodium carbonate is treated with benzenesulfonyl chloride. The rearrangement, which may be represented as follows,

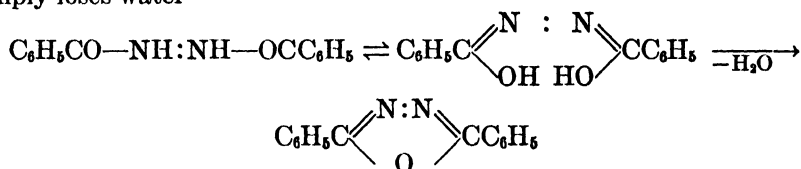


involves in effect the augmentation of a benzoic acid to a carbonic acid and the simultaneous reduction of hydroxylamine to ammonia and water.

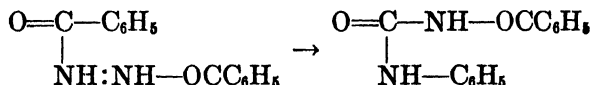
Acylhydrazides

As has already been noted, it is only occasionally that an alkyl or alkylidene derivative of hydrazine reacts in a manner interpretable as involving the nitridizing action of the hydrazine group. So with the decomposition of the acid derivatives of hydrazine, it is in a few cases only that hydrazine nitrogen undergoes reduction, thereby functioning as a nitridizing agent.

Symmetrical dibenzoylhydrazine, $\text{C}_6\text{H}_5\text{CO}-\text{NH}:\text{NH}-\text{OCC}_6\text{H}_5$. Gilbert (29) has shown that this compound, when heated for a time at 350°C ., simply loses water



to form a cyclic dibenzoic hydrazide. When however the compound, in successive small portions, is suddenly subjected to a temperature of 450°C ., good yields of aniline, phenyl cyanide, and carbon dioxide are obtained. The formation of these compounds may be explained by assuming that dibenzoylhydrazine undergoes rearrangement into *N*-phenyl-*N'*-benzoyl-urea



and that this compound decomposes at high temperatures to yield the compounds named above.

Gilbert found also that *sym*-benzoyl-*p*-tolylhydrazine and benzoyl-*p*-chlorobenzoylhydrazine undergo decomposition in a manner resembling that of dibenzoylhydrazine.

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CHLOROPICRIN

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INTRODUCTION

In the writing of this monograph an attempt has been made to provide a summary of the work done with chloropicrin (also known as trichloronitromethane and nitrochloroform) and to include all the important work done on this subject up to and including the year 1931. As chloropicrin is used principally as a repellent, fumigant, insecticide, parasiticide, and disinfectant, the literature has been difficult to search, for not infrequently the name does not appear in the title of the paper or in the index of the journal in which the paper is published.

PREPARATION

Chloropicrin was first prepared by Stenhouse (1), who added an aqueous solution of picric acid to an excess of bleaching powder. Considerable study was given to its preparation and the following methods were worked out: by boiling picric acid with potassium chlorate and hydrochloric acid; by boiling picric acid with aqua regia; by bubbling chlorine through a hot aqueous solution of picric acid; by heating potassium picrate with a solution of bleaching powder; by boiling Dammara resin with nitric acid and then treating the resulting product with bleaching powder; by digesting in nitric acid the resinous compound which chlorine formed with usnic acid; by boiling chrysamic acid, styphnic acid, or Erdmann's oxypicric acid with either bleaching powder or potassium chlorate and hydrochloric acid.

Kekulé (2) obtained chloropicrin by the action of alcohol and concentrated nitric acid upon sodium chloride and also (3) by the distillation of solid or liquid chloral with concentrated nitric acid, or with a mixture of nitric and sulfuric acids; or, when a mixture of methyl alcohol and sulfuric acid was distilled with a mixture of sodium nitrate and sodium chloride.

Hofmann (4) prepared chloropicrin by a modification of Stenhouse's (1) original method by making a thick cream with ten parts of fresh bleaching powder, after which it was mixed with a saturated solution of one part of picric acid warmed to 30°C.; as soon as the violent reaction was completed, chloropicrin was distilled over.

Mills (5) prepared chloropicrin by the nitration of chloroform, by heating seven volumes of chloroform with sixteen volumes of nitric acid (containing much nitrogen peroxide) in a sealed tube to 90°–100°C. for 120 hours. It was recommended that the tube be kept at an angle of 30° with the bottom of the bath, as it appeared that a more nearly horizontal position involved the destruction of any nitro compound that may be formed, while an upright position caused the reaction to proceed with excessive slowness.

Green and Rowe (6) found that when sodium hypochlorite was used as an oxidizing agent with dinitroaniline, nitro-*p*-phenylenediamine, nitroacetyl-*p*-phenylenediamine, and the azo compound obtained by combining diazotized nitro-*p*-phenylenediamine with β -naphthol, the ring was ruptured and chloropicrin formed. They also found (7) that when 2,4-dinitronaphthylamine was subjected to hypochlorite oxidation, either in suspension or in alcoholic solution, at the ordinary temperature or when cooled with ice, disruption of the ring resulted, accompanied by a strong odor of chloropicrin, but the compound was not capable of isolation.

Datta and Chatterjee (8) were able to obtain an 85 per cent yield of chloropicrin when acetone was added to ten parts of a slightly warmed mixture of two parts of nitric acid and three parts of hydrochloric acid, warmed for some time on the water bath, and then steam distilled. When allyl alcohol was gradually added to a mixture of the acids (2:3) with occasional warming on the water bath, its transformation was complete. In like manner ether and ethyl alcohol were converted into chloropicrin. And, as the result of extensive investigations, they found (9) that whenever an organic compound broke up destructively under the influence of aqua regia, chloropicrin was invariably produced.

Datta and Fernandes (10) have shown that chloropicrin is formed from hydrocarbons which undergo decomposition by aqua regia (cymene, styrene, diisobutylene, triisobutylene, etc.).

Copisarow (11) in the utilization of trinitrotoluene residues found that chloropicrin could be obtained by the employment of Hofmann's method, and, considering the percentage of nitrogen present, found that the yield compared favorably with that obtained by the degradation of picric acid residues.

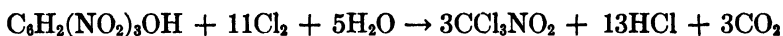
Orton and Pope (12) obtained, on May 9, 1918, British patent No. 142,878 for the preparation of chloropicrin by the action of chlorine on picric acid or on other suitable nitro derivatives of a phenol or of a naphthol in the presence of water and a basic material, such as metallic oxides, carbonates, or borates, preferably sodium or potassium hydroxides or carbonates, to dissolve the nitro derivatives and neutralize the acid produced in the reaction. The basic material may be added in successive stages or wholly at the beginning.

King (13) obtained, on January 13, 1920, U. S. patent No. 1,327,714 for a process of producing chloropicrin which consists in forming an admixture of bleaching powder with water, wherein the amount of water is six times the equivalent of lime, and adding thereto a solution of calcium picrate.

Orton and McKie (14) were able to obtain a yield of chloropicrin reaching 200 per cent by passing chlorine into a cooled suspension of sodium picrate in aqueous sodium carbonate. Picric acid was dissolved in a hot solution of four parts of sodium carbonate (17 equivalents) in fifty parts of water. The thin paste was rapidly cooled to below 5°C. (to produce small crystals), and chlorine added slowly or intermittently (too rapid a stream of chlorine not only wastes the gas but in addition produces chlorates). The products are chloropicrin and some nitric acid, together with chloride and some hypochlorite, and chlorate which has arisen from transformation of hypochlorite. For determinations of the hypochlorite, chlorate, and chloride in the aqueous product, it was found that the proportion of the last accords well with the opinion that chloropicrin was formed in a reaction between hypochlorite (hypochlorous acid) and picric acid, thus:



that is,



when the maximum yield would be 215 per cent, or,



where the maximum yield would be 143.5 per cent.

Frahm (15) obtained chloropicrin in theoretical amounts by using the less expensive alkali, lime, and carrying out the reaction at 0°C.

Sweeney (16) obtained, on April 18, 1922, U. S. Patent No. 1,413,198 for a process of making chloropicrin by bringing together, under pressure, a suspension of a chlorine-yielding material in water and suspensions of picric acid and lime in water. Oxidation loss and foaming are suppressed.

Chloropicrin has been produced by the action of chlorine upon an aqueous solution of sodium nitranilate and iodine (17); by the action of chlorine on silver fulminate (18); by heating chloroform with acetylnitrate (19); by refluxing dihydro-s-chlorxylol with 30 per cent nitric acid (20); as a by-product when the chloro derivatives of 5-nitrobarbituric acid were formed (21); when 2,4-dichloroacetanilide was warmed with concentrated nitric acid (22); by the action of sodium hypochlorite on nitrophenols (23); by the action of chlorine on 1,3,5-trinitro-2,6-dihydroxybenzene (24); by the oxidation of trichloronitrosomethane (25).

PHYSICAL PROPERTIES

Freshly distilled chloropicrin is a colorless liquid which becomes yellow in diffused light and in sunlight assumes the color of nitrous vapors (26). The boiling point has been determined by several observers. Stenhouse (1) determined it as 120°C. and Hofmann (4) as 112°C.; neither value can be taken as correct, whereas both might be, as the observers did not record the pressure at which their determinations were made. Bertrand (27) gave it as 112.3°C. at 766 mm. and 15°C. at 30.2 mm. Cossa (28) determined its boiling point as 112.8°C. at 743 mm. and Thorpe (29) observed it to be 111.91^A (^Aair thermometer degree) (corrected) at 751.9 mm., a value which Piutti (26) checked. Blaszkowska-Zakrzewska (30) calculated it as 112.21°C. at 760 mm.

Chloropicrin solidifies in a freezing mixture at -64°C. (31), and at -69.2°C. (corrected) (32). It crystallizes in the shape of long, thin needles possessing a strong double refraction and a parallel extinction, thus belonging to the tetragonal, hexagonal, or orthorhombic systems. No other polymorphic modifications have been observed above -200°C. (33).

The density of chloropicrin at 16°C. was determined as 1.666 (27). The specific gravity at 0°/0° as 1.69247, at 4°/4° as 1.69225 (29), at 20°/4° as 1.6539 (34), at 4°/4° as 1.6855, at 10°/10° as 1.6748, at 15°/15° as 1.6670, at 20°/20° as 1.6594, at 25°/25° as 1.6528 (35).

Chloropicrin is almost insoluble in water. At 0°C. the solubility is 0.2272 g. per 100 cc. of water; at 25°C., 0.1621 g.; at 75°C., 0.1141 g. At 32°C. 100 g. of chloropicrin dissolves 0.1003 g. of water; at 41°C., 0.1243 g.; at 55°C., 0.2265 g. Thus it is shown that chloropicrin is only slightly soluble in water, the solubility decreasing with increase of temperature; water is only slightly soluble in chloropicrin, the solubility increasing with increase in temperature (36). The values obtained are given in tabular and graphical form in tables 1 and 2, also figures 1 and 2.

Chloropicrin dissolves iodine, cinnamic acid, benzoic acid, resins, etc. It is miscible in all proportions with benzene, amyl alcohol, carbon disulfide, and absolute alcohol. At 11°C. one volume of 80.55 per cent alcohol dissolves 3.7 volumes of chloropicrin; one volume of 78 per cent alcohol dissolves 1.3 volumes; one volume of ether dissolves 0.3 volume (28).

A sample of Kahlbaum's chloropicrin dried over calcium chloride and distilled at 111°-111.5°C. under 750.5 mm. showed the following refractive indexes at 22.8°: 1.45740 (Li), 1.45793 (H_a), 1.46075 (Na), 1.46393 (Ti), 1.46785 (H_b), 1.47377 (H_γ) (34).

Chloropicrin dried over phosphorus pentoxide and distilled from anhydrous potassium carbonate at 112°C. showed an average specific magnetic rotation at 12.7°C. of 0.9843, and a molecular rotation of 5.384 (35). For more complete values see table 3.

TABLE 1
Solubility of chloropicrin in water

	TEMPERATURE		
	0°C.	25°C.	75°C.
Grams chlorine in 100 cc. water.....	0.1472	0.1060	0.0739
	0.1465	0.1048	0.0753
	0.1468	0.1049	0.0695
	—	0.1049	0.0674
	—	0.1042	0.0796
	—	0.1055	0.0768
Average equivalent of chloropicrin.....	0.2272	0.1621	0.1141

TABLE 2
Solubility of water in chloropicrin

WATER	CHLOROPICRIN		TEMPERATURE OF MISCIBILITY	WATER PER 100 GRAMS OF CHLOROPICRIN
<i>grams</i>	<i>cc.</i>	<i>grams</i>	<i>degrees C.</i>	<i>grams</i>
0.1098	29.3	48.49	55.0	0.2265
0.1098	35.8	59.25	50.8	0.1853
0.1098	40.3	66.70	48.0	0.1647
0.1098	53.4	88.38	41.0	0.1243
0.1098	56.0	92.68	36.0	0.1185
0.1098	66.0	109.25	32.0	0.1003

TABLE 3
Specific magnetic rotation and molecular rotation of chloropicrin

TEMPERATURE	SPECIFIC ROTATION	MOLECULAR ROTATION
<i>degrees C.</i>		
15.6	0.9800	5.376
15.6	0.9804	5.378
15.6	0.9800	5.376
15.6	0.9775	5.363
15.6	0.9810	5.382
9.0	0.9905	5.399
9.0	0.9887	5.389
9.0	0.9905	5.399
9.0	0.9899	5.395
Average...12.7	0.9843	5.384

The specific conductivity of chloropicrin was found to be at least ten times less than that of nitromethane, less than 6×10^{-3} reciprocal ohms (37).

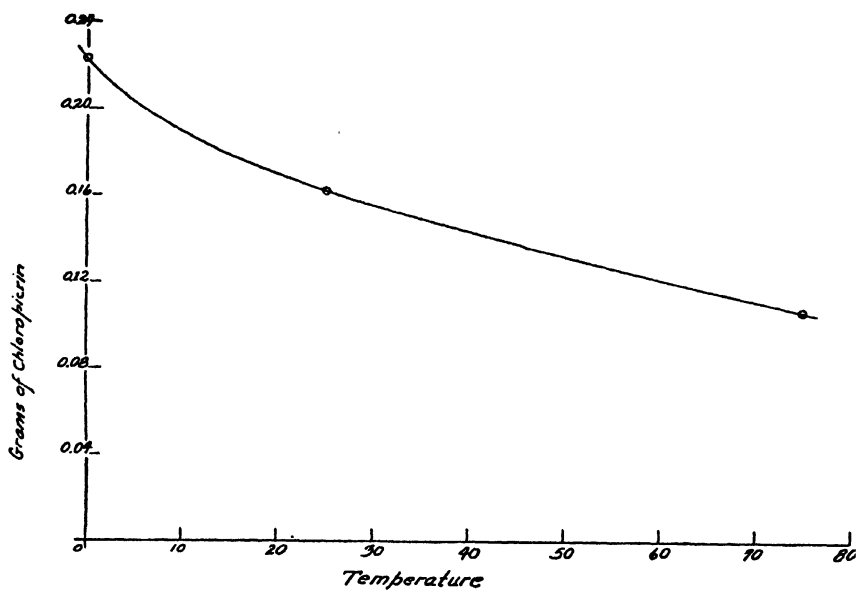


FIG. 1. SOLUBILITY OF CHLOROPICRIN IN 100 GRAMS OF WATER

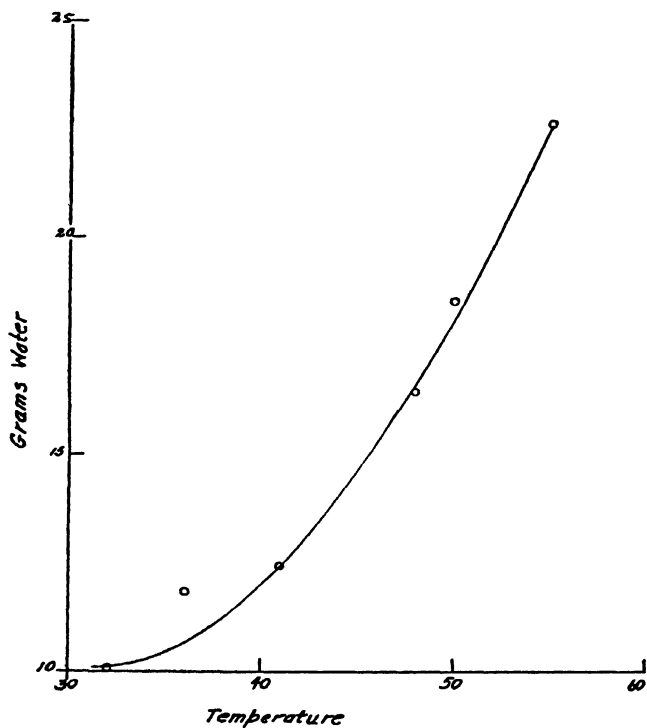


FIG. 2. SOLUBILITY OF WATER IN 100 GRAMS OF CHLOROPICRIN

Cotton and Mouton (38) determined that chloropicrin has a positive magnetic birefringence of 2.0606 at 14.2°C.

The molecular diamagnetism of chloropicrin was shown by Pascal (39) to be 785, which is 115 less than the calculated value. Not only with this compound but in all cases in which two or more halogens are attached to the same carbon atom, quite a discrepancy was found. This was supposed to be due to the formation of double bonds between the halogens as demanded by Thiele's theory.

By means of the formula developed by Kleeman (40)

$$\gamma - t(dy/dt) (M_v)^{2/3} = 2.38 (T_c - t)$$

where γ = surface tension, t = temperature, and T_c = critical temperature, Bennett and Mitchell (41) calculated the total surface energy for chloropicrin from the data of Schiff (42) and determined it as 1535, the theoretical value being 1558.

The molecular depression of the freezing point of chloropicrin in formic acid varied from 25.7 to 27.4, indicating no dissociation (43). The results on a series of nitrogen derivatives show that the aromatic compounds are all more or less dissociated, while those of the aliphatic series are not. The authors account for this dissociation by supposing the formation of an additive product of the type $R-NO(OH)(COOH)$; one fact in favor of this hypothesis is that solutions of aromatic polynitro derivatives in anhydrous formic acid are colorless even at high concentrations, while with other solvents, whether possessed of dissociating power or not, they form intensely yellow solutions.

The optical absorption of chloropicrin is very similar to that of nitromethane as found by Hantzsch and Voigt (44). Thus it is to be noted that the substitution of chlorine for hydrogen brings about but a very slight effect.

Thorpe (29) calculated the relative volume of chloropicrin. The observations given in table 4 were made with dilatometer in the water bath. Observations made in an oil bath are given in table 5.

These observations may be represented by the formula

$$3378.99 + 3.632970t + 0.00148070t^2 + 0.000026430t^3$$

which gives the numbers in the last columns of tables 4 and 5. Dividing through by the first term and correcting for the expansion of the glass (0.00002553), this expression becomes

$$V = 1 + 0.0011007t + 0.000000465757t^2 + 0.000000007833t^3$$

by the aid of which table 6, showing the relative volume of chloropicrin at every 5° between 0° and 110°, is calculated.

TABLE 4
Expansion of chloropicrin in water bath

Δ°	RELATIVE VOLUME	
	Observed	Calculated
00.00	3378.8	3379.0
10.21	3416.2	3416.3
19.11	3449.4	3449.1
30.66	3492.5	3492.5
40.15	3529.1	3528.9
49.98	3567.5	3567.6
59.67	3606.6	3606.7

* Temperatures expressed in air-thermometer degrees, which are distinguished, in order to prevent confusion, by Bergamm's symbol for fire or heat.

TABLE 5
Expansion of chloropicrin in oil bath

T°	t°	T	V	E	VOLUME	
					Observed	Calculated
70.50	23.5	70.43	3638.7	247.0	3651.7	3651.4
80.31	25.4	80.38	3676.1	284.7	3694.3	3694.3
89.25	28.3	89.46	3711.7	320.3	3734.7	3734.8
102.81	30.4	103.32	3766.3	374.9	3799.4	3799.3
107.84	31.8	108.44	3786.8	395.4	3823.9	3824.1

TABLE 6
Relative volume of chloropicrin between 0^{Δ} and 110^{Δ}

Δ	VOLUME	DIFFER- ENCE	Δ	VOLUME	DIFFER- ENCE	Δ	VOLUME	DIFFER- ENCE
0	100000	—	40	104528	585	80	109505	657
5	100552	552	45	105119	591	85	110174	669
10	101016	554	50	105718	599	90	110855	681
15	101664	558	55	106325	607	95	111549	694
20	102226	562	60	106941	616	100.00	112256	707
25	102793	567	65	107567	626	105.00	112978	722
30	103365	572	70	108202	635	110.00	113714	736
35	103943	578	75	108848	646	111.91	113999	—

By combination with van't Hoff's equation for E , the molecular rise of boiling point, the equation

$$E = 0.001115T^2/\alpha_i^2$$

was derived, and using the data of Schiff (42). Walden (45) calculated the

specific cohesion of chloropicrin at its boiling point as 2.82. From the equation

$$\lambda_s = 46a_s/\log T_s$$

the latent heat of vaporization was calculated as 50.2 calories per gram.

Aston and Ramsay (46), from the molecular surface energy and its variation with temperature, found chloropicrin to have a normal molecular weight.

Baxter, Bezzenberger, and Wilson (47) determined the vapor pressure of chloropicrin by the "air current" or "transference" method. A known volume of air, as determined by the measured volume of water run out of an aspirator, was saturated with the vapor of chloropicrin by passing through a weighed receptacle maintained at constant temperature in a water thermostat. The loss in weight of the saturating tube furnished the weight of evaporated substance. From the latter quantity the volume of vapor was calculated on the assumption that the volume of a gram molecule under standard conditions is 22.41 liters. The per cent of vapor by volume multiplied by the interior pressure, as determined by the barometric reading and an open-arm water manometer attached to the aspirator, gives the vapor pressure. The control of temperature in the thermostat was within 0.1°C. except when a freezing mixture was employed, where the uncertainty may have been as large as 1°C. at -18°C.

A plot of the logarithm of the vapor pressure against the reciprocal of the absolute temperature gives a very nearly straight line, which therefore, can be represented by an empirical equation of the form

$$\log \text{vapor pressure} = A + B/273 + t$$

Satisfactory values of A and B were computed.

Vapor pressures calculated by means of these equations agree with the observed values within the experimental error. For a higher degree of accuracy the equations were not adequate, however, and can not be trusted for extrapolation over any considerable range.

The original chloropicrin was distilled in a partial vacuum in two portions. The first was used at 35°, 25°, 15°, and 0°C.; the second at the other temperatures.

$$\log \text{vapor pressure} = 8.2424 - 2045.1/273 + t$$

The data in table 7 furnish evidence from which the heats of vaporization may be computed. Using the Clausius-Clapeyron equation

$$L = T \, dp/dt (V_{\text{gas}} - V_{\text{liquid-solid}})$$

and values for the vapor pressures calculated from the logarithmic vapor pressure equations, the results are expressed in kilogram-calories per gram molecule. The heat of vaporization is 6.77 at 35°C. and 7.10 at 0°C.

The vapor tension of chloropicrin was determined (30) from 98°C. to 105°C. in Swietoslawski's ebullioscopic thermostat by the "air current" method. The apparatus consists of a 500- to 600-cc. flask connected by a narrow tube with the thermostat proper, a cylinder of 55 mm. diameter which carries a thermometer, a siphon fused into the bulb of the flask and a reflux condenser; the latter is connected with the pressure regulating system. The apparatus in which the air current is saturated with the vapors was constructed by Wojnicz-Sianozecki and resembles Gahl's wash bottle (48). The velocity of the air current was 300 cc. per minute. The

TABLE 7
Vapor pressure of chloropicrin

TEMPERATURE	VOLUME OF AIR AT 0°C. AND 760 MM.	LOSS IN WEIGHT OF SATURATION TUBE	INTERIOR PRESSURE	VAPOR PRESSURE (Observed)	VAPOR PRESSURE (Calculated)	DIFFERENCE (Calcd. - observed)
°C.	cc.	grams	mm.	mm.	mm.	mm.
35	2185	0.9222	736.9	40.14	40.04	-0.10
30	2434	0.7571	764.5	31.10	31.10	0.00
25	2670	0.6428	749.5	23.81	23.97	0.16
20	2184	0.3963	759.1	18.31	18.30	-0.01
15	2972	0.4053	756.6	13.82	13.85	0.03
10	2745	0.2790	758.2	10.37	10.37	0.00
0	2559	0.1468	735.3	5.71	5.64	-0.07
-18	3299	0.0611	754.1	1.90	1.67	-0.23
-19	3400	0.0566	751.5	1.70	1.55	-0.15
-20	3125	0.0459	751.8	1.50	1.44	-0.06

mean error was 0.6°-0.8°C. The values obtained were 502.1 at 98°C., 532 at 100°C., 564.4 at 102°C., 567.6 at 103°C., 583 at 104°C., and 597 at 105°C.

The "immersed bulb" method (49) permits determinations of vapor tension with very small amounts of material (0.03 to 0.05 g.) and with greater accuracy than by the "air-current" method. The bulb was placed in the ebullioscopic thermostat for the determination of the vapor pressure of chloropicrin from 97°C. to 105°C. The following values were obtained: 491.4 at 98°C., 524.3 at 100°C., 558.2 at 102°C., 557.9 at 103°C., 595.2 at 104°C., and 612.8 at 105°C. These results differ considerably from those obtained by the "air-current" method and may be considered more trustworthy, because of the experimental errors inherent in the latter (too high velocity of the air current and carrying over of liquid drops) and because

Avogadro's law, which underlies the calculations of vapor tension by the dynamic method, probably does not obtain for saturated vapors. The curve

$$\ln p - 1/T$$

is a straight line, or

$$\ln p = A - (B/T)$$

where $A = 7.8704$ and $B = 1921.4$. Baxter, Bezzenburgh, and Wilson (47) however, determined $A = 8.2424$ and $B = 2045.1$, and stated that the

TABLE 8
Freezing points of binary mixtures of chloropicrin and nitrogen peroxide

CHLOROPICRIN	NITROGEN PEROXIDE	TEMPERATURE AT WHICH MELTING	
		Started	Finished
<i>per cent</i>	<i>per cent</i>	<i>degrees C.</i>	<i>degrees C.</i>
100	0	-64.0	-64.0
95	5	-72.0	-79.5
92	8	-79.5	-79.5
89	11	-67.5	-79.5
70	30	-42.5	-79.5
50	50	-27.5	-67.5
30	70	-18.0	-30.0
20	80	-15.0	-23.5
10	90	-12.0	-16.0
0	100	-10.2	-10.2

equations were not adequate over any considerable range. Hertz's equation (50)

$$\ln p = \alpha - (\beta/T) - (\gamma \ln T)$$

where $\alpha = 18.3014$, $\beta = 2485.5$, and $\gamma = 3.468$, covers the entire temperature interval from 0°C. to the boiling point, and the calculated results agree well with the experimental ones.

Pascal (51) determined the freezing point of a series of binary mixtures of chloropicrin and nitrogen peroxide as shown in table 8.

At 32°C. and under a pressure of one atmosphere, 3.4 pounds of chloropicrin can exist in the vapor phase in a 1000 cu. ft. chamber (52).

Flury (53) determined the volatility of chloropicrin as 175,000 cu. mm. per cubic meter.

Lecat (54) formed azeotropic mixtures with chloropicrin (b.p., 111.85°C.) and a number of compounds (see table 9). Nonazeotropes formed with toluene and acetal.

Allyl alcohol, dimethylethylcarbinol, normal butanol, and isobutylcarbinol form positive azeotropes with chloropicrin; methyl alcohol and normal hexanol form nonazeotropic systems with chloropicrin (55).

Chloropicrin and sixty-two other halogen-containing organic compounds were used by Tronov (56) in making a study of the activity of the halogens. A small quantity of a halogen compound was taken to react with about one mole of pyridine or piperidine in a sealed tube and the product of the reaction titrated with silver nitrate. As the result of these investigations it was found that the mobility diminishes from iodine to bromine and chlorine. This difference was considerable with aliphatic but less with aromatic compounds. The mobility of a halogen decreases with the increase in length of the hydrocarbon chain and the proximity of a side chain. A primary is more mobile than a secondary halogen. The proximity of a double bond decreases the mobility of a halogen compound. Oxygen increases the mobility of $C:O > \text{oxide } O > OH$. The influence on

TABLE 9
Azeotropic mixtures of chloropicrin with other compounds

CHLOROPICRIN	COMPOUND	BOILING POINT OF AZEOTROPIC MIXTURE
<i>per cent</i>		<i>degrees C.</i>
35.0	Ethyl alcohol (b.p., 78.3°C.)	77.4
33.5	Isopropyl alcohol (b.p., 82.45°C.)	82.0
58.5	Propyl alcohol (b.p., 97.2°C.)	94.0
67.5	Isobutyl alcohol (b.p., 107.85°C.)	102.05
29.0	Methyleyclohexane (b.p., 101.1°C.)	100.75

the mobility of a halogen atom of other halogen atoms in the molecule is more complicated. But even in this case it has been noticed that the splitting takes place more readily the more positive the radical is.

Harned (57), making measurements of the velocity of adsorption of chloropicrin at 20°C. by wood charcoal (14 to 16 mesh) which contains 6 per cent non-volatile material, showed that there is sometimes an initial lag in adsorption, and that in all cases discordant and unreproducible results are obtained except when the reaction is proceeding at the maximum velocity obtainable under a given set of temperature and pressure conditions. At the maximum velocity, adsorption occurs in accordance with the equation

$$\log K = \log A - B/t$$

where K is the weight of the gas in grams per gram of charcoal adsorbed in time t , and A and B are constants. The velocity constant is given by the expression

$$m = (1/t) \log [A/(A - K)]$$

The results obtained with chloropicrin indicate that a tenfold decrease in pressure has been found to cause a forty-twofold decrease in m ; at higher pressures the capacity of charcoal varies but little with pressure. Thus, the capacity per gram of charcoal amounts to 0.2800 g. at a pressure of approximately 5×10^3 bars and to 0.3100 g. at 5×10^4 bars. The data agrees qualitatively with the one-layer theory regarding the capacity as developed by Langmuir (58). (See table 10 and figure 3.)

TABLE 10
Adsorption of chloropicrin by charcoal

$p = 5.90$ mm.; t = time of exposure in seconds; K = weight of gas adsorbed per gram of charcoal in time t

I		II		III	
t	K	t	K	t	K
1.6	0.0030	1.6	0.0056	2.2	0.0091
3.2	0.0070	2.8	0.0082	5.4	0.0221
5.7	0.0116	5.1	0.0159	8.6	0.0374
9.1	0.0241	7.4	0.0234	13.8	0.0568
14.4	0.0418	9.7	0.0305	24.3	0.0753
25.1	0.0636	15.0	0.0479	6600.0	0.1854
463.0	0.1578	25.4	0.0728		
		503.0	0.1406		

I. Weight of charcoal = 0.8420 g. Heated to 350°C. for 2 hours in a high vacuum, cooled and maintained at $20^\circ \pm 1^\circ\text{C}$. The tube containing chloropicrin was kept in ice water. By keeping the liquid reservoir at a temperature lower than the charcoal, distillation was avoided.

II. Same charcoal, same weight as in I. No air or moisture was permitted to come into contact with the charcoal between measurements I and II. Reheated to 350°C. for 2.5 hours in a high vacuum. Gain in weight of charcoal equalled 10 mg. Same temperature conditions during velocity measurements as in I.

III. Same charcoal. Reheated to 350°C. for 7 hours in a high vacuum. No foreign gas admitted. Gain in weight of charcoal equalled 1.5 mg. Same temperature conditions as in I and II.

Adsorption decreases with rising temperature (59). This temperature effect is slight at higher pressures, but much more pronounced at lower pressures. The variation of adsorption with temperature also increases as the boiling point of the gas is approached.

Moisture is more highly adsorbed at ordinary temperature by charcoal than any other of the normal constituents of the air. On the other hand, it is much less adsorbed than such toxic gases as chloropicrin for instance. Thus an active charcoal will adsorb and retain 25 per cent of its own weight of chloropicrin at 20°C. and will adsorb an approximately equal amount of

water if it is exposed to saturated water vapor at the same temperature, but it holds this water very feebly, losing all but 1 or 2 per cent of it when it is exposed to dry air for some time. Figure 4 a shows the effect of humidity on the adsorption of chloropicrin by a rather poor sample of charcoal at 20°C.

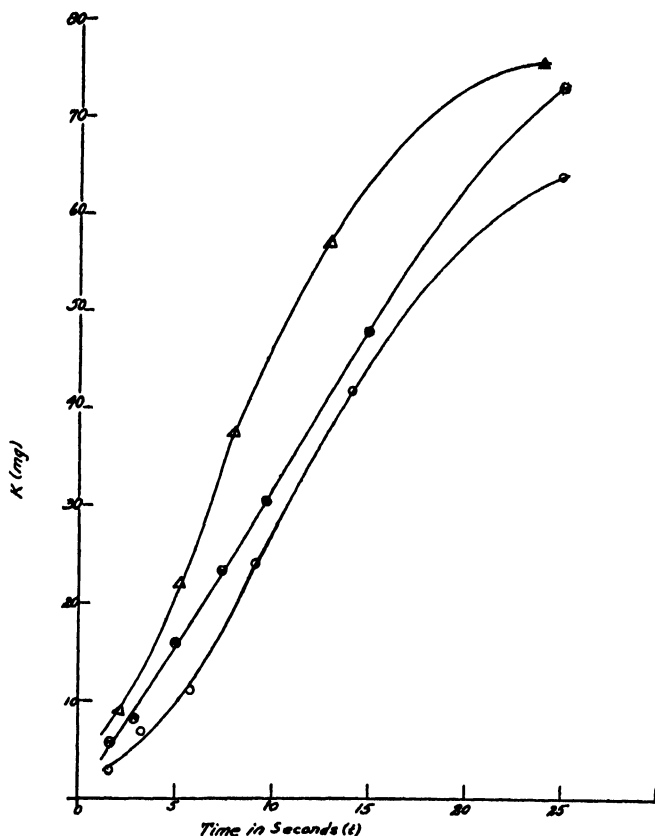


FIG. 3. ABSORPTION OF CHLOROPICRIN BY CHARCOAL

$p = 5.90$ mm.; t = time of exposure in seconds; K = weight of gas absorbed per gram of charcoal in time t .

The dynamic activity of an adsorbent layer is characterized by the time of protective action, which is defined as "the time from the beginning of flow of gas to the moment when the gas appears on the exit side of the adsorbing layer." Dynamic activity of charcoal is usually detected by passing a stream of air containing a small amount of chloropicrin through the charcoal. The method of Dubin, Solov'ev, and Shilin (60) of deter-

mining the "moment of jump" of the stream of gas after passing through charcoal is by allowing the issuing gas to pass through a tube bent at a right angle at the end and placed just above, but not touching, the surface

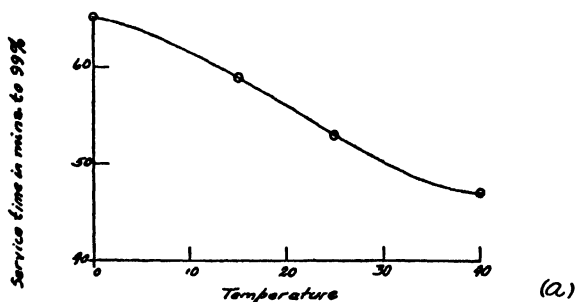


FIG. 4a. EFFECT OF TEMPERATURE ON SERVICE TIME TO 99 PER CENT EFFICIENCY OF CHLOROPICRIN AT 0.7 PER CENT CONCENTRATION OF DRY AIR

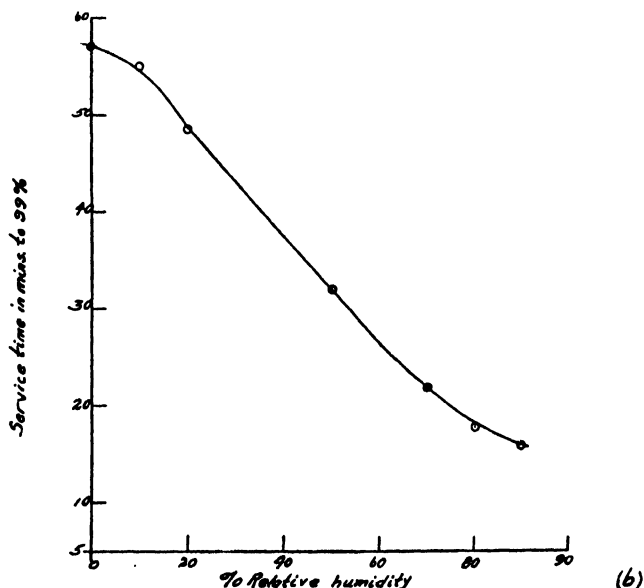


FIG. 4b. EFFECT OF HUMIDITY OF GAS-AIR ON SERVICE TIME OF EQUILIBRATED CHARCOAL AGAINST CHLOROPICRIN CONCENTRATION
Concentration, 0.7 per cent; depth of layer, 10 cm.

of a starch-iodide solution. A piece of filter paper dipping into the solution is placed in front of the tube so that when chlorine is present in the issuing air stream it produces the characteristic mark on the wet filter paper. This method is described as exceedingly delicate.

Chloropicrin is best adsorbed by dyed new wool and dyed used silk, while linen is the poorest adsorbent (61).

Results of experiments (62) have left no doubt that small concentrations of chloropicrin are adsorbed very quickly when exposed to comparatively large rubber or rubberized surfaces. A strip of sheet rubber, 1 in. \times 8 in., was suspended in an adsorption bulb, a known amount of gas was then put into the bulb, and the gas allowed to remain in contact with the rubber for time intervals ranging from 15 minutes to 16 hours. At the end of the selected interval the residual gas was drawn through the adsorbing solution and analyzed (see figure 5).

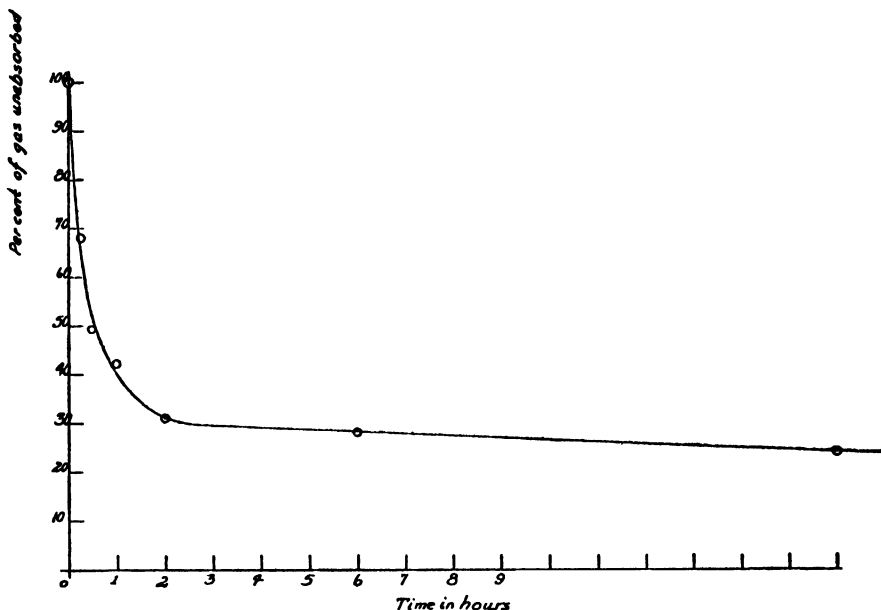


FIG. 5. ABSORPTIVE POWER OF RUBBER FOR CHLOROPICRIN

Volume of bulb, 1000 cc.; area of rubber, 8 square inches; concentration of chloropicrin, 650 p.p.m. initial.

Bouyoucos (63) determined the heat of adsorption of chloropicrin by using active charcoal which had been de-ashed and outgassed at 900°C. and obtained the results as shown in table 11.

Blażkowska-Zakrzewska (64) determined that at about 140°C. a drop of chloropicrin evaporated on an aluminum bronze surface in minimum time. This is characteristic and depends on the nature of the surface. The evaporation begins by increasing with the rise in temperature, reaches a definite maximum, and afterwards decreases. This decrease of the rate of evaporation with further rise of temperature is produced by the so-called

spheroidal state of the liquid, known as Leidenfrost's effect. The spheroidal state evidently impedes evaporation, since in this state liquid no longer wets a given surface.

CHEMICAL PROPERTIES

Auwers and Harres (65), using the spectrochemical method, confirmed the usually accepted structure of a normal nitro compound for chloropicrin.

At its boiling point chloropicrin slowly decomposes into carbonyl chloride and nitrosyl chloride.



It was determined by Gardner and Fox (66) that 200 cc. of chloropicrin, held at its boiling point, decomposes at the rate of 2 cc. per day.

TABLE 11
Heat of adsorption of chloropicrin at 0°C.

<i>A</i>	<i>Q</i>	$\Delta Q/\Delta A$
<i>cc.</i>	<i>joules</i>	
0.307	20.84	67.9
0.672	42.48	59.3
1.012	59.89	51.2

A = total amount of gas adsorbed per gram of adsorbent reduced to standard conditions.

B = total amount of heat (expressed in millijoules) evaporated by the adsorption of *A*.

At 100°C. chloropicrin is decomposed rapidly by sulfuric acid containing 20 per cent of the anhydride, into phosgene and nitrosyl chloride. A 73 per cent yield may be obtained in 35 minutes (67).

Solutions of chloropicrin in ethyl alcohol, methyl alcohol, benzene, turpentine, acetic acid, etc., remain unchanged in the dark, but when exposed to light all except those in the alcohols become colored. The solutions in alcohols, after one day, separate into two layers, and white crystals of ammonium chloride separate at the bottom. Acetone solutions are somewhat colored and do not separate in two layers, but deposit ammonium chloride. Evidently the alcohols reduce the NO_2 to NH_2 and then to NH_3 . Reductions by alcohol in light were observed by Ciamician and Silber (68) and others, but this instance is striking because the NH_2 is reduced only in the light. The alcohol or acetone solutions may be boiled in the dark and remained unchanged (26).

Piutti (69) further showed that when certain compounds are present with chloropicrin, decomposition of the latter by light is accompanied by

oxidation, chlorination, or nitration of the other compound, depending on its nature. Solutions of chloropicrin in acetic acid (m.p., 16.5°C.) turned yellowish brown and separated into two layers in one day; in the lower layer crystals of formic acid separated in one month, and increased in amount for six months. The lower layer, on distillation from 90–115°C., yielded unaltered chloropicrin. Aqueous extracts of the distillate and of the residue contained chlorine, hydrochloric acid, nitrous acid, and unaltered acetic acid. The upper layer, distilled at 128°C., yielded fractions containing these same compounds, but when distilled in vacuum for 40 minutes at approximately 84°C., monochloroacetic acid was recovered. Equal parts of diethyl succinate and chloropicrin after 4 days exposure to light precipitated a crystalline mixture of succinic acid with a small amount of oxalic acid which increased in amount for one month. With equal volumes of methyl salicylate and chloropicrin a mixture of 1,2,3-methylchlorosalicylate (m.p., 48°C.), oxalic acid, ammonium tetroxalate, and a brown resin first appeared in five days and increased in amount for one year. Equal volumes of toluene and chloropicrin first turned yellow, then brown; after two months oily drops appeared, and after five months both large white and minute colorless crystals. Fifty grams of toluene and 50 g. of chloropicrin gave, after seven months, 13.2 g. of benzoic acid, some oxalic acid, and a brown liquid. The latter separated into two layers, containing hydrochloric acid and *o*-nitrotoluene. A mixture of naphthalene and chloropicrin turned brown after four days, and became lighter in twenty days with the appearance of crystals. The latter increased for three and one-half months and yielded 4.34 g. of benzoic acid and 3.79 g. of phthalic acid from 50 g. of naphthalene and chloropicrin.

Chloropicrin decomposes under the action of ultra-violet light. The products are at first nitrosyl chloride and phosgene, but the latter splits into carbon monoxide and chlorine (70).

Kling and Florentin (71), basing their work on that of Gardner and Fox (66), showed that chloropicrin decomposes slowly into nitrosyl chloride and phosgene, a reaction permitting the supposition that this body is susceptible of taking the tautomeric form $\text{O}:\text{N}-\text{O}:\text{C}:\text{Cl}_2$.



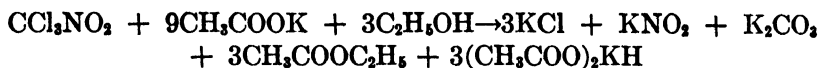
When hydrogen chloride is passed through chloropicrin at 100°C. and the mixed vapor passed through a tube filled with pumice and heated to 400°C., the bulk of the chloropicrin is decomposed into phosgene, nitrosyl chloride, and nitric oxide, but a small portion is converted into hexachloroethane (72).

On heating chloropicrin to 100°C., in contact with copper, brass, tin, cadmium, zinc, aluminum, lead, and iron the decomposition is slight, but at the boiling point of chloropicrin the rate of decomposition is increased

tenfold (73). The rate of decomposition is practically proportional to time. The catalytic effect of iron and lead is smallest while that of brass is greatest.

The action of chloropicrin on smooth metallic surfaces at room temperature is very slight; the activity is increased if the atmosphere is humid, yet the metals are not completely destroyed. Alekseevskii and Alekseev (74) explain this by supposing that the metals gradually acquire passivity.

When chloropicrin is heated to 100°C. in a closed vessel with fused potassium acetate and alcohol, decomposition takes place with great ease (75).



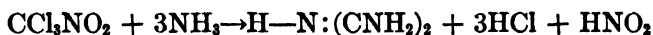
On heating a mixture of one part of chloropicrin with three parts of aniline to 145°C. a violent reaction takes place and carbtriphenyltriamine is formed.

By the action of metallic sodium on a solution of chloropicrin in absolute alcohol, ethyl orthocarbonate is obtained (76).



Chloropicrin and sodium methylate react vigorously to form tetramethyl orthocarbonate (77).

By heating chloropicrin with a strong alcoholic solution of ammonia in an autoclave at 100°C. for several hours, guanidine is obtained (78).



When chloropicrin is heated in a sealed tube with fuming hydriodic acid, the following reaction takes place (79).



By the action of potassium cyanide upon chloropicrin in dilute alcohol, dinitrilechloronitromalonate is formed (80). When chloropicrin is digested with a concentrated, warm solution of potassium bisulfite, it is largely converted into potassium nitroformicdisulfonate (81). In the presence of anhydrous aluminum chloride, chloropicrin and benzene react to form triphenylmethane and triphenylcarbinol (82). By the action of zinc methyl upon chloropicrin, tertiary nitrobutane is obtained; by the action of zinc ethyl upon chloropicrin, nitroheptane, secondary nitropentane, and primary nitropropane are formed (83).

The products of the reduction of chloropicrin seem to vary with the nature of the reducing agent. With stannous chloride and hydrochloric

acid (84), trichloronitromethane is produced which, in turn, decomposes into cyanogen chloride and hydrogen chloride. The occasional formation of traces of ammonia was noticed but, as a rule, after removing the tin by means of hydrogen sulfide, the product was found to be free from ammonium chloride and the hydrochlorides of hydroxylamine and methylamine. Iron filings and acetic acid (85) or tin and hydrochloric acid (86) give rise to monomethylamine.



Owing to the importance of methylamine in synthetic organic chemistry and to the fact that chloropicrin was easily obtained in large quantity from gas shells, it appeared to Frankland, Challenger, and Nicholls (87) desirable to investigate more closely its reduction. By employing fine iron filings and hydrochloric acid it was found that the composition of the reduction product depended upon the conditions of the experiment. The use of iron and hydrochloric acid in the theoretical quantities (six atomic proportions of iron and nine molecular proportions of acid to one of chloropicrin) in such a way as to prevent the formation of ferrous or ferric hydroxides gave a product rich in ammonium chloride. If chloropicrin is shaken with iron filings and water, the mixture becomes extremely hot and a vigorous reaction sets in, which, however, gradually slackens if no acid is added. By adopting the method employed in the reduction of aromatic nitro compounds or of nitromethane and nitroethane (88), the reaction proceeds satisfactorily in the presence of only about one-fortieth of the theoretical amount of hydrochloric acid, and a practically theoretical yield of methylamine hydrochloride is obtained.

It would thus appear that the formation of methylamine by reduction is due to reaction of chloropicrin as such, whereas ammonia is to be regarded as derived from the decomposition products (89).

Henderson and Macbeth (90) demonstrated that titanous chloride reduced the nitro group in chloropicrin and left the halogen unattacked.

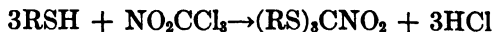
When chloropicrin is condensed with ethyl sodiomalonate and with ethyl sodiocyanoacetate, the products formed are ethyl ethanetetra-carboxylate or ethyl α, α' -dicyanosuccinate, respectively (91).

At ordinary temperatures calcium iodide and chloropicrin do not react, but at 45°C. a reaction begins with the separation of iodine (92). Chloropicrin causes copper to dissolve rapidly in concentrated ammonia water (93).

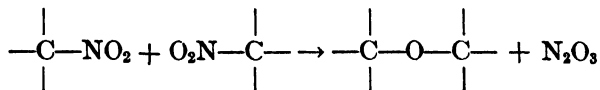
Chloropicrin is attacked but slowly by alkaline solutions of hydrazine and only one chlorine atom is removed. It was found that the quality of the chloropicrin had a great effect on the reaction, as a sample which had been freshly distilled under reduced pressure gave qualitative results (94).



Chloropicrin reacts readily with mercaptides: at ordinary temperatures the reaction is



while at higher temperatures the reaction proceeds further.



It has been recommended that chloropicrin be used as a reagent for the diagnosis of mercaptans and potential mercaptans (95).

Nekrassow and Melnikow (96) have shown that chloropicrin acts as an oxidizing agent with the simplest mercaptans. Ethyl mercaptan, thio-phenol, and thio-*p*-cresol give with chloropicrin products which the molecular weight determinations confirmed as the corresponding disulfides, rather than as condensation products of high molecular weight. With ethyl mercaptan there is obtained, instead of Ray's product melting at 123°C., a substance melting at 151.5°C.; this is apparently diethylenetetrasulfide or some oxidation product of $(\text{CH}_2\text{SH})_2$. With mercaptides there is always a considerable evolution of gas consisting, along with carbon dioxide, chiefly of nitrogen with not inconsiderable and approximately equal amounts of carbon monoxide and nitric oxide. The main reaction is represented by the equation,



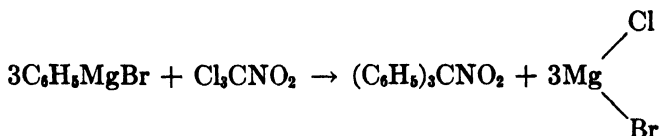
and is accompanied to a smaller extent by the reaction



The reaction with the free mercaptans is very slow, but the potassium mercaptides react immediately even in the cold, and as the resulting disulfides are practically insoluble in water, the reaction can be used to detect traces of chloropicrin in aqueous solutions. Phenyl mercaptan is especially well adapted for this purpose; with 0.01 mg. of chloropicrin in 1 cc. of water, made faintly alkaline, a few drops of alcoholic thiophenol produce an opalescence and with higher concentrations a precipitate.

The interaction of chloropicrin and phenol in the presence of potassium hydroxide results in the elimination of the nitro group, which effects oxidation and is itself reduced to ammonia. The principal products are *o*- and *p*-salicylic aldehyde, and the corresponding acids. Large quantities of *p*-rosolic acid are also formed, probably by condensation of the phenol with the salicylic aldehyde (97).

The reaction of chloropicrin with phenylmagnesium bromide takes place as follows and is accompanied by a brilliant green fluorescence (98).



The action of methylmagnesium iodide on chloropicrin, and on other nitro compounds, gave more gas than the equivalent of one active hydrogen, the amount of which varied with the reaction time. Gilman and Fothergill (99) attributed the gases formed to the presence of the nitro group and not to active hydrogen, since nitro compounds containing no hydrogen (as chloropicrin) still yielded them.

Alkali polysulfide solutions destroy the odor of chloropicrin. A yellow color is obtained when a drop of chloropicrin is boiled with alcoholic potassium hydroxide and a small quantity of thymol. The substitution of resorcinol for thymol produced a red color. The addition of sulfuric acid to the thymol mixture produced a reddish violet color, and the whole mixture on dilution with acetic acid exhibited an absorption band in the green portion of the spectrum. Chloropicrin forms carbylamine. Chloropicrin when boiled with potassium hydroxide solution gives, after cooling, reactions characteristic of nitrous acid (100).

When iodine and potassium iodide dissolved in methyl alcohol are poured together and allowed to stand in contact with chloropicrin, the following reaction takes place (101):



With one, two, or three moles of potassium iodide to one mole of chloropicrin there is obtained carbon tetraiodide but no iodine-substituted chloropicrin. Analogous results are obtained in ethyl alcohol and benzene; the reaction, however, proceeds with a greater speed without the use of solvents.

Elbs and Wittich (102) prepared ditolylmethane and tritolylmethane by distilling a mixture of chloropicrin and toluene, diluted with an equal volume of carbon bisulfide, with zinc dust.

DeForcrand (103) prepared from chloropicrin a compound having the formula $\text{CCl}_3\text{NO}_2 + 2\text{H}_2\text{S} + 23\text{H}_2\text{O}$.

Gardner and Williams (104) obtained, on March 13, 1922, British patent No. 198,462 for the employment of chloropicrin as a nitro oxidizing agent in place of nitrobenzene in the synthesis of quinoline and its derivatives which are, in turn, used in the preparation of Alizarin Blue and other dyes.

Trumbull and Evans (105) obtained, on March 1, 1922, U. S. patent No.

1,402,195 for a process of making crystal violet in which chloropicrin and dimethylaniline are used.

When 10 g. of chloropicrin and 30 g. of dimethylpyridine are mixed in a hermetically sealed flask and left standing at room temperature for eight days, the nitro group of chloropicrin is first split off and the nitration of dimethylpyridine takes place, as indicated by the appearance of a cherry red coloration after twenty-four hours. The chlorine is split off and the first signs of formation of methyl violet appear after three to four days. The liquid thickens, darkens, and finally crystallizes, while the odor of chloropicrin disappears (106).

Backer and Klaassens (107) prepared the anhydrous dipotassium salt of nitromethanedisulfonic acid by gradually adding 82 g. of chloropicrin to 450 g. of potassium sulfite in 900 cc. of water, heated to 75°C., and keeping the temperature at 80°C.

Chloropicrin slowly oxidizes potassium iodide to iodine and hemoglobin to methemoglobin (108).

Chloropicrin gives with amines and many hydrocarbons colored addition compounds (109). The results indicate that the colored compounds result from the interaction of subsidiary valencies associated with the NO_2 group on the one hand and with the C:C or the N atom on the other. In general, it appears that the production of color, in the case of nitro compounds, is always a consequence of the saturation of the subsidiary valencies of the NO_2 group.

Cuprous chloride in concentrated ammonium hydroxide colors chloropicrin first green, then dark blue in two to three minutes, and finally results as a yellowish precipitate (110).

DETECTION

An aqueous solution of chloropicrin reduced with metallic calcium gives some nitrous acid, shown by the red precipitate with β -naphthylamine and sulfuric acid. The reaction is sensitive to 0.002 mg. per liter but not suitable for a quantitative determination (111).

Chloropicrin is easily detected (qualitatively) with a test paper which has been previously soaked in a dilute solution of dimethylaniline in benzene. In the presence of chloropicrin there is a momentary fading, according to the concentration, from bright yellow to dark brown.

For a quantitative determination the chloropicrin-air mixture is drawn through glacial acetic acid in a spiral wash flask and reduced by nascent hydrogen generated from iron. After filtering, it is strongly acidified with nitric acid and precipitated with silver nitrate and the chlorine determined according to Volhard. A second method is accomplished by the thermal decomposition of the air drawn through a glass tube filled with potassium

carbonate and heated to 300–500°C. The chlorine is determined as before (112).

PHYSIOLOGICAL ACTION

Flury (113) determined man's toleration limit for chloropicrin to be 60 cu. mm. per cubic meter of air and Hanslian (114) states that 2400 mg. of chloropicrin per cubic meter of air will kill a man if breathed for 1 minute.

Exposure to chloropicrin causes lachrymation, coughing, nausea, and vomiting, and, in large quantity, it may cause unconsciousness. Secondary effects are bronchitis, shortness of breath, a weak irregular heart beat, and gastritis; it may also lead to acute nephritis. The detrimental influence of this agent is confined to the respiratory tract, and all the other effects must be regarded as secondary; the epithelium of the respiratory tract is injured, the medium and small bronchi being most affected. There is a uniform widespread damage of the alveolar walls, which, however, is not severe enough to lead to necrosis. The alveoli are apparently nowhere protected by constriction of the bronchi. Overwhelming edema of the lungs rapidly follows exposure to the lethal concentration of the gas. In extreme cases practically every alveolus is filled with fluid. The direct cause of death is the extreme concentration of the blood which is brought about by edema (115).

Liquid chloropicrin has a corrosive action on the skin, and scratches and abrasions exposed to chloropicrin fumes invariably become septic. Abscess formation may result (116).

The most efficacious method of treatment in chloropicrin poisoning is to bleed one-half of one per cent of the body weight as soon as possible after gassing and then to administer at once water by way of the mouth. Additional fluid may be supplied later by intravenous infusion of sodium chloride solution in accordance with hemoglobin readings and temperature changes. With this treatment there are no delayed deaths (117).

USES

One milligram of chloropicrin in one liter of sugared must retards fermentation, and 5 to 6 mg. stops fermentation entirely. One milligram per liter will prevent the growth of *Saccharomyces vini* (118). Twenty to 30 mg. of chloropicrin per liter stops lactic acid fermentation; 50 to 60 mg. of chloropicrin per liter stops the ammoniacal fermentation of urine; and 0.1 mg. of chloropicrin per liter stops all development of the bacteria of sorbose (119).

Mercandier (120) found chloropicrin to be bactericidal to *B. coli* and streptococcus; a saturated atmosphere of chloropicrin kills the bacilli in less than twenty-four hours in the light at the temperature of the labora-

tory. The spore of *B. anthracis* is killed in a saturated atmosphere of chloropicrin in from six to fourteen hours at 17–18°C., whereas *B. subtilis* is only slightly attacked after forty-eight hours.

An aqueous solution of chloropicrin (1.6 g. per liter) was found by Violle (121) to possess high antiseptic power. At the rate of 12 mg. per liter of bouillon, chloropicrin prevents the growth of *B. coli*, *B. typhosus*, *B. paratyphosus*, staphylococcus, streptococcus, and other non-spore-forming bacteria. At the rate of 24 mg. per liter of bouillon, chloropicrin prevents the growth of *B. subtilis*. Emulsions of *B. coli*, *B. typhosus*, *B. paratyphosus*, *B. dysentericae*, *B. proteus*, and *B. pyocyaneus* are killed after a 30-minute contact with chloropicrin, and *B. subtilis* is killed after contact for one hour. Chloropicrin retains its bactericidal power for several hours (in contradistinction to chlorine, iodine, and their derivatives) and does not coagulate egg albumen and other protein bodies.

Randier (122) showed that cultures of *B. paratyphoid*, *B. Yersin*, and *B. Eberth* failed to grow after having been exposed to chloropicrin vapor.

When tested by the wet filter paper method, Reddish (123) found that chloropicrin killed both *B. typhosus* and *M. aureus* in 15 minutes.

It was found by Shuffelebotham (124) that chloropicrin was very effective against *B. influenzae*.

A great deal of experimentation has been done with chloropicrin on insects and favorable results have been reported on the following: *Acarapis woodi* (125), *Agriotes* (126), *Agriotis segetum* (127), *Aleurobius farinae* (128), *Aleyrodes vaporariorum* (129), *Anobiids* (130), *Anobium hirtum* (131), *Anopheles maculipennis* (132), ants (133), aphids (134), arachnid (131c), *Argas reflexus* (135), *Blattella germanica* (136), *Bombyx mori* (137), *Bombyx neustria* (138), *Bruchus chinensis* (139), *Bruchus obtectus* (140), Buffalo carpet beetle (141), cabbage root fly (134b), *Calandra granaria* (142), *Calandra oryza* (143), *Callipterus italicus* (144), *Ceratophyllus fasciatus* (145), *Cerocipidae* (127b), *Ceroplastes rusci* (146), *Charancons* (147), *Chrysomyia macellaria* (148), *Cimex lectularius* (149), *Cochliomyia macellaria* (150), *Coræbus rubi* (151), *Criocephalus rusticus* (152), *Culex pipiens* (132), *Dendrolimus pini* (136d), *Dermestes vulpinus* (153), *Diaspis pentagona* (146), *Dociostaurus maroccanus* (154), *Doryphora* (155), *Echocerus cornutus* (156), *Ectobia lividia* (157), *Ephestias* (147a), *Ephestia kuehniella* (158), *Epitrix cucumeris* (129), fleas (159), flies (160), fur parasites (159c), *Galleria mellonella* (161), *Gelechia gossypiella* (152), *Geometrid larvae* (127b), grain insects (162), grasshoppers (163), *Heterodera* (164), *Hylotrupes bajulus* (152), *Jassidae* (127b), *Laemophaeus ferrugineus* (165), *Laemophaeus minutus* (129), *Lecanium hesperidum* (146), *Lepism* (166), *Leptinotarsa decemlineata* (167), *Leucotermes lucifugus* (168), *Liparis chryssorrhoea* (146), *Lucilla* (150b), *Malacosoma neustria* (136d), *Melolontha*

vulgaris (169), *Microgaster glomeratus* (170), *Monomorium pharaonis* (171), *Muca domestica* (172), *Myzus persicae* (129), *Nematodes* (173), *Nuptus hololeucus* (174), *Otiorhynchus cingulatus* (166), *Otiorhynchus sulcatus* (175), *Oxythyrea hirta* (170), *Pachymerus chinensis* (129), *Palomona viridissima* (166), *Pectinophora gossypiella* (176), *Pediculus humanus* (177), *Periplaneta* (136), *Phlorimaea operculella* (152), *Phorbia ceparum* (134b), *Phthorimaea operculella* (176), *Phyllodromia germanica* (136d), *Pieris brassicae* (170), *Pieris rapae* (166), *Platyedra gossypiella* (178), *Plodia americana* (179), *Plodia interpunctella* (180), *Polychrosis botrana* (181), *Rhizopertha dominica* (129), rice insects (182), scale (134c), *Schistocerca tatarica* (144), *Silvanus surinamensis* (183), *Sirex juvencus* (152), *Sitodrepa panicea* (127b), *Sititroga cerealella* (184), *Souris* (147), *Sparganothis pilleriana* (134b), *Stephanoderes coffea* (185), *Strachia conata* (166), *Tar-*

TABLE 12

Action of chloropicrin on fungi

	TIME						
	7 min-utes	15 min-utes	30 min-utes	60 min-utes	210 min-utes	340 min-utes	480 min-utes
<i>Amblyosporium</i>					—	—	+
<i>Botrytis cinera</i>	—	—	—	—	+	+	+
<i>Chaetomium bostrychodes</i>					—	—	+
<i>Hypomyces ochracea</i>	+	+	+	+	+	+	+
<i>Mucor mucedo</i>	—	—	—	—	+	+	+
<i>Nocardia</i>	—	—	—	—	—	—	+
<i>Penicillium</i>	—	—	—	—	—	—	+

+ indicates that death of the organism resulted from that exposure.

sonemus (129), *Tenebrio molitor* (186), *Tenebrionid* (166), *Tenebroides mauritanicus* (187), *Tenthredinid* (178), tent caterpillar (188), *Tetranychus bumaculatus* (189), *Tetranychus telarius* (190), thrips (127b), timber insects (191), *Tinea granella* (192), *Tinea pellionella* (157), *Tineola bisellieella* (193), *Trialeurodes vaporariorum* (194), *Tribolium confusum* (195), *Tribolium ferrugineum* (129), *Tribolium navale* (196), *Trichophaga tapetzella* (157), *Trogoderma granarium* (197), *Trogoderma khapra* (198), *Tyroglyphus farinae* (139), *Tyroglyphus mycophagus* (195a), weevils (199).

Matruchot and See (200) obtained the results shown in table 12 using a saturated atmosphere of chloropicrin on the fungi growing in culture tubes.

Bertrand (201) found that chloropicrin has the same effect upon plants in the dark as in diffused daylight, but in the direct sunlight the injury is much greater. Humidity does not affect the activity of chloropicrin vapor on plants. The influence of temperature is very distinct. If the differ-

ences of treatment are too great, the effects of chloropicrin are almost proportional to the concentration of the vapor and the duration of the exposure; that is, a 20-minute exposure to a concentration of 30 g. gives the same result as a 30-minute exposure to 20 g. Tests were made with the leaves of the following species: Japanese spindle tree, black poplar, lilac, pear tree, elm, melilot, and golden daisy.

Chloropicrin has been used successfully as a fumigant on a number of other plants: apple tree (202), aster (127b), beans (134b), begonia (127b), cabbage (134b), camelia (146), coleus (127b), cottonseed (176), daisy (127b), dandelion (127b), date (203), dock (127b), edible mushroom (204), geranium (127b), Japanese spindle wood (27), jasmine (146), legumes (169), myrabolan (146), onions (134b), orange tree (205), plum tree (206), poplar (138), potatoes (152), roots (126b), rose (207), saliva (127b), tomato plants (208), vine grafts (169), weeds (209), willow boughs (127b), wild cherry (134c), wild quince (146), wild vetch (127b).

Cats gassed with chloropicrin in such concentrations that death generally results within 4 days usually exhibit a marked generalized analgesia, both superficial and deep. Gassed cats react with no obvious sign of pain to operative interferences, including laparotomy and gentle friction of the parietal peritoneum. The analgesia develops within a few hours after gassing and reaches its maximum in about twenty-four hours. With chloropicrin practically normal sensitiveness has been observed seven days after gassing. This analgesia is considered to be caused and maintained largely by a general, low-grade tissue asphyxia, which is chiefly of pulmonic origin. In most instances death occurred within forty-eight hours after gassing, 1 part to 10,000, for 30 to 60 minutes (210).

Winternitz, Finney, and Wislocki (211) show the comparative toxicology of chloropicrin for the rabbit, dog, cat, monkey, goat, rat, and guinea pig. Florentin (212) determined the toxic dose of chloropicrin for a dog to be 0.5 gram.

Experiments made with goats, sheep, and cattle on the ranges have shown that small quantities of chloropicrin in mineral oil, or in pine tar oil, are very effective in repelling flies, and that wounds treated with the mixture appear to heal rapidly (213).

Earthworms and millipedes were killed to a depth of 5 inches in soil after exposure for 1.5 hours to a concentration of chloropicrin, 8.7 oz. per 1000 cu. ft. at 55.4°F., relative humidity at 88 (127). Chloropicrin is of great value as a partial sterilizing agent. It is fatal to eelworms and wireworms and harmless to plants; indeed, it promotes root action to a remarkable degree (214).

Bertrand and Dassonville (215) recommend that chloropicrin be substituted for sulfur dioxide in the treatment of mange (gale) in horses. Excellent results are said to be obtained.

A water solution of chloropicrin (10 to 20 mg. per liter) is very toxic to amoeba, vorticella, and paramecium. It is suggested that chloropicrin be used for partial sterilization of stools (134a).

Field mice have been successfully exterminated by Ringelmann (216) and Vayssi re (217) with the use of chloropicrin. Rats have been successfully exterminated by the use of chloropicrin (218). Encouraging results have been obtained by Lormand (219) in tests with chloropicrin for the destruction of foxes and by Traunt (220) in the extermination of the Siberian marmot.

A viper resisted the action of chloropicrin at the rate of 30 cc. per cubic meter for 7 minutes, then died (170).

Billon (221) obtained, on October 16, 1926, French patent No. 612,075 for the purification of vaccines by means of chloropicrin.

Chloropicrin has been recommended for use as a warning agent for illuminating gas or with hydrocyanic acid when used as a fumigant (222).

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THERMAL REACTIONS OF TERPENE HYDROCARBONS¹

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¹ Presented before the Organic Division at the Eighty-fourth Meeting of the American Chemical Society at Denver, Colorado, August 23, 1932.

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I. INTRODUCTION

The terpenes are among the more important substances present in essential oils, the complex mixture of cyclic and acyclic compounds obtained from many plants and trees.

A detailed discussion of the composition of a great number of essential oils is outside the scope of this paper, but it is of interest to note some recent studies to illustrate their complexity. Rutovski and Vinogradova (125) have found that the essential oil of *Nepeta Cataria* contains tiglic acid, α - and β -citral, limonene, dipentene, a levorotatory sesquiterpene, geraniol, citronellol, nerol, and acetic, butyric, and valeric acids. Ikeda and Fujita (82a) report that the essential oil of *Cunninghamia kinoshii*

TABLE 1
Turpentine and rosin produced in the United States

YEAR	TURPENTINE	ROSIN
	<i>gallons</i>	<i>barrels</i>
1929	35,600,000	2,453,000
1930	35,837,000	2,455,000
1931	27,100,000	1,900,000
1932	22,000,000	1,600,000

Hayata contains pinene, sabinene, limonene, α -terpenol, *l*-borneol, and *d*-cedrol.

Crude mineral oils from which terpenes have been isolated include those from Galicia, Rumania, Grozny, Baku, Canada, Beaumont, Texas, and Java. Engler and Hofer (45) state that Java oil is particularly rich in terpenic compounds. A South Africa crude oil consisted almost entirely of acyclic compounds with limonene and sylvestrene predominating. Upon evaporation the gasolines yielded a product much like gum arabic in appearance.

However, the only major industry engaged primarily in the production of terpenes is that of turpentine and rosin (115), which started many centuries before Christ when the natives of Asia manufactured pitches and oils from the gum of trees which grew along the shores of the Mediterranean. In the United States the production of crude resin from pines and the making of pitch and tar began in the early part of the seventeenth century. At that time, the gum was gathered from the pines of Virginia

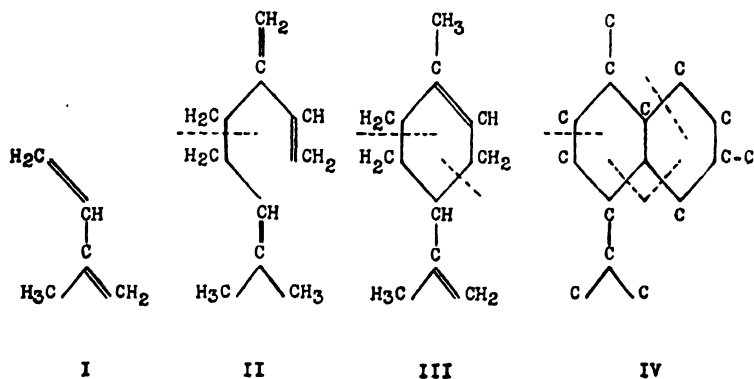
and North Carolina. Today, about two-thirds of the world's turpentine and rosin are produced in the southern states. Table 1 (177) shows the amount of these materials produced in the United States.

The importance of the industry is apparent upon consideration of the everyday uses into which turpentine enters. As a thinner of oil varnishes and gloss paints, for example, gum spirits of turpentine has no superior. It may be an ingredient of printing inks and is used for color-printing processes in lithography; in the manufacture of cotton and woolen print goods; in the manufacture of patent leathers; a thinner for waxes in shoe and leather polishes, and floor, stove, and furniture polishes; a solvent for waterproofing compositions, and for rubber and similar substances; an ingredient in belting greases; an insecticide; in laundry glosses, in washing preparations, in sealing wax and in pharmaceuticals, including disinfectants, liniments, soaps and ointments; and a raw material for producing synthetic camphor, and, indirectly, celluloid and explosives.

II. GENERALIZATIONS

The substances ordinarily considered in a discussion of the terpenes are the hemiterpene, isoprene (C_5H_8), the true terpenes, having the general formula $C_{10}H_{16}$, the sesquiterpenes of formula $C^{15}H_{24}$, the higher or polyterpenes, $(C_5H_8)_n$, and their various derivatives.

Simonsen (155) points out the relationship existing between isoprene and the higher terpene hydrocarbons, simple and complex. The latter may be considered as being made up of two or more isoprene molecules. Thus two molecules of isoprene, C_5H_8 (I) are contained in the molecule of the true terpenes, e.g., myrcene (II) and limonene (III), while the sesquiterpenes represented by formula IV contain three, and the higher terpenes contain more such nuclei.

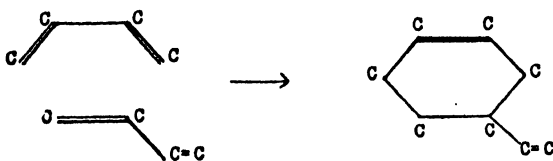


Isoprene, a hemiterpene, is diolefinic and its thermal reactions are those to be expected of such a compound. At lower temperatures the principal change that it undergoes is one of polymerization to higher terpenic compounds. As the temperature is increased, decomposition takes place with the formation of ethylene, propylene, butadiene, etc., and at still higher temperatures aromatic compounds appear. Staudinger, Endle, and Herold (158) consider that the formation of aromatic substances is due to the polymerization of isoprene to hydroaromatic derivatives which, by further polymerization or condensation with isoprene, give products of high molecular weight. These mixtures of terpenes and polyterpenes then decompose into the aromatic compounds.

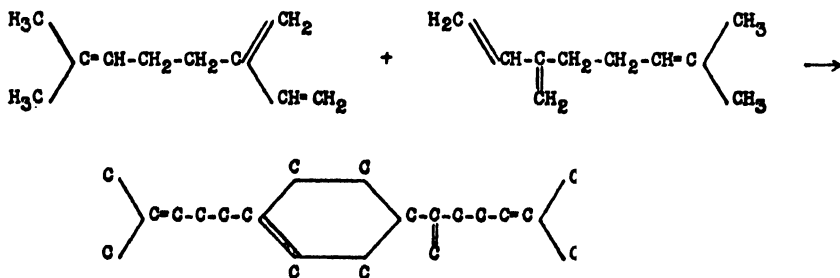
The polymerization of isoprene results in a complex mixture of terpenic substances ranging from simple terpenes to rubber. Some of the many simpler intermediates, which have been isolated and identified, are the same as naturally occurring terpenes, but others are not.

Whitby and Katz (190) have suggested that the most plausible mechanism for the polymerization of unsaturated compounds is "best represented as proceeding stepwise by the addition regularly of successive molecules of monomer to the double bond present at each stage of the polymerization immediately preceding." This, of course, applies to any olefinic compound.

The dimerization of isoprene, according to Wagner-Jauregg (182), proceeds as shown below:



This represents 1,4-addition and is of "general significance for the polymerization of hydrocarbons with conjugated double bonds. As a further example, the polymerization of myrcene to α -camphorene may be cited" (152).



Gapon (52), discussing the mechanism of polymerization of diolefinic hydrocarbons, draws the following conclusions, based upon the assumption that activation, in the presence of polymerization, consists essentially in the breaking of a double bond and the transformation of quadrivalent carbon atoms into trivalent carbon atoms: (1) The theoretical value of the energy of activation is the energy required to break one double bond, in the absence of chain reactions. (2) Activated molecules react with normal ones to give products of polymerization, although they can not react among themselves.

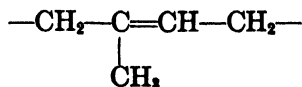
He also claims to have differentiated three second-order reactions in the polymerization of isoprene at 100–105°C. that occur simultaneously; two dimers, dipentene, and 1,3-dimethyl-1-vinyl-3-cyclohexane are formed together with a complex polymer. These three processes are seemingly so clearly differentiated that he further gives as the activation energies for the three reactions, 22,400, 21,500, and 18,800 calories, respectively.

The contention of Kassel (87) that the formation of polyatomic molecules by a second-order association process is possible at a relatively large fraction of all collisions has received support from the experiments of Vaughan (178) on measurements of the hydrogenation of ethylene and the dimerizations of ethylene and of 1,3-butadiene. Evidence was also obtained indicating that the orientation of the properly activated particles at the moment of impact is highly important for the achievement of reaction, and that the more complex the molecules the more precise must be their mutual locations.

Later experiments by Vaughan (179) on the dimerization of isoprene have served to bear out the above conclusions. In addition, working in the temperature range of 286.5°C. to 371°C. at pressures varying from 212 to 739 mm. the principal process, dimerization, was interpreted as a bimolecular association reaction.

The mechanism of polymerization of olefins which seems to be regarded the more favorably is that which involves the dissociation of hydrogen and comparatively simple addition to the double bond of another molecule. For example, Carothers (35) discusses the polymerization of ethylene as follows: "In effect at least this reaction involves in the first step the addition of ethylene, as $\text{H}- + -\text{CH}=\text{CH}_2$, to the double bond of another molecule of ethylene, and then a similar addition to butylene."

Although the structural unit in the polymeric chain from isoprene appears to be



and Midgley and Henne (104) obtained three dimers of isoprene, each of which contains two such units, Carothers has pointed out that Midgley's results "by no means prove that the actual mechanism of the reaction consists in the direct union of radicals corresponding in formula with the structural unit. The 1,4-addition of $\text{H}- + -\text{CH}=\text{C}(\text{CH}_3)\text{CH}=\text{CH}_2$ to isoprene, for example, would lead to the same result."

The reactions of myrcene, an acyclic terpene, should be quite similar to those of isoprene and, in so far as they are known, this seems to be true. However, the present status of our knowledge of the thermal behavior of myrcene leaves much to be desired.

A glance at the structure of any of the cyclic monoterpenes would indicate that their thermal reactions are very complex, for these compounds are cycloolefins with unsaturated side chains. It would be interesting to compare the results of the studies of monocyclic monoterpenes with those of other substituted cyclic olefins, but a survey of the literature has shown that no study of the non-catalytic decomposition of cyclohexene or cyclohexadiene at a temperature above 300°C. has been published. Only one case has been reported in which the ring was broken, and this was a catalytic decomposition to hydrogen, paraffinic gases, and aromatics. One study is insufficient to use as a basis of comparison, but it is interesting to note how frequently isoprene, which must result from ring breaking, has been reported as a product of decomposition of monocyclic terpenes. Little is known of the other decomposition products.

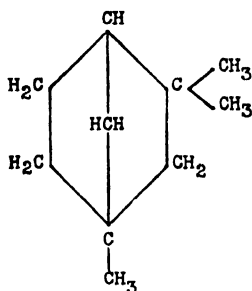
Like other cyclohexene derivatives, the monocyclic terpenes undergo simultaneous hydrogenation and dehydrogenation in the presence of catalysts, yielding cyclohexyl and aromatic compounds.

In the case of dicyclic and tricyclic monoterpenes which may contain tri-, tetra-, or penta-methylene rings as well as a cyclohexene ring, the primary reactions would be expected to be dependent upon the relative stability of the two rings. In the case of the pinenes, the thermal decomposition products are quite similar to those of monocyclic terpenes. For example, Mahood (99) has pointed out that pinene yields considerable quantities of terpenic substances when "cracked" at temperatures below 400°C., while aromatic hydrocarbons and olefins, including isoprene, are the chief constituents of all fractions obtained at higher temperatures. This seems to indicate that the cyclobutane ring breaks before other reactions set in.

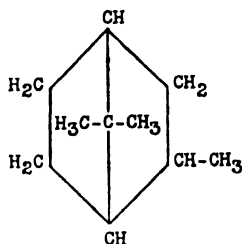
On the other hand, thujene, which contains a trimethylene ring, appears to be decomposed in the presence of catalysts in such a way that both the tri- and hexa-methylene rings are broken by the severing of one linkage, the product being a pentamethylene derivative.

Fenchane (I), isobornylane (II) and α -fenchene (III), all of which con-

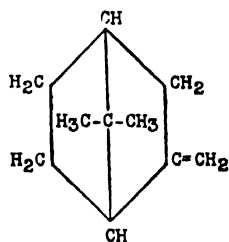
tain a pentamethylene ring, remain unchanged under conditions which result in the decomposition of thujene and pinene.



I



II



III

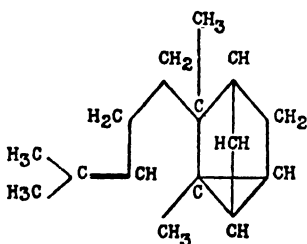
As a result of their work on the catalysis of bi- and tri-cyclic systems, Zelinsky and Lewina (199) make the following generalizations: "On catalytic hydrogenation, the bi- and tri-cyclic systems of terpene hydrocarbons are easily broken and hydrogen is absorbed. On catalytic dehydrogenation, however, the breaking of these rings leads to the formation of unsaturated hydrocarbons, and in case these form an unsaturated hydroaromatic compound, complete dehydrogenation occurs; if the unsaturated hydrocarbon is a cyclopentane derivative, no further dehydrogenation takes place."

Of course, the sesquiterpenes and diterpenes present an even more complex picture than the monoterpenes, for they may have several rings, or one ring with a long unsaturated side chain, or they may be acyclic. However, no work has been found concerning the thermal reactions of any acyclic sesquiterpenes and the work that has been done on the other types of compounds is quite meager. The studies have resulted chiefly in rearrangements, hydrogenation, and dehydrogenation rather than in more deep-seated changes.

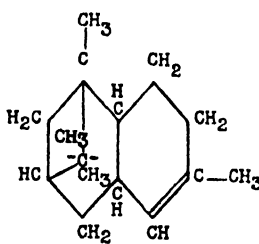
Ruzicka and his coworkers have dehydrogenated sesquiterpenes by refluxing them with sulfur. If the compound contains a hydrobenzene ring, the product is a benzene derivative having the same side chains as the original. The same relationship holds for hydronaphthalene derivatives provided there are no substituents on those carbon atoms which are common to both rings. In the latter case such substituents are removed as mercaptans.

It is worthy of note that of all the sesquiterpenes which yield naphthalene compounds on dehydrogenation with sulfur, not one is thought to contain a tri-, tetra- or penta-methylene ring. On the other hand caryophyllene, cedrene, santalene, and clovene, all of which contain one or more rings

smaller than the hexamethylene ring, have been studied, but none has been found to yield naphthalene hydrocarbons.



Santalene (130b)

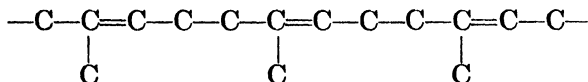


Clovene (74)

In fact, cedrene remains unchanged and the other three yield dehydrogenation products which were not identified further than to prove that they were not naphthalene derivatives. Furthermore, Nakatsuchi (110) has found that pinene, which contains a tetramethylene ring, yields a polymerized product and $C_{10}H_{16}S$, but no *p*-cymene.

At first glance it may seem that rubber is not a terpenic substance, for its most salient characteristics are not typical, but fundamentally it is a polyterpene, for its empirical formula is $(C_5H_8)_n$. Furthermore, the fact that it, along with terpenes and sesquiterpenes, is a product of polymerization of isoprene, and that it decomposes yielding terpenes and isoprene, definitely links it with terpenic substances.

There is a great amount of literature on the subject of the structure of rubber and no structure can be said to have been proven. The preponderance of evidence (163), however, is in favor of the long chain molecule



which Pickles (117) first suggested. A compound of this structure should be expected to behave as other polyolefinic compounds, and that has been found to be true in the case of rubber. The linkage which seems to be most easily broken is that farthest removed from the double bonds, so that of the acyclic compounds formed on pyrolysis, those containing five carbon atoms to the molecule predominate. However, compounds containing six or seven atoms of carbon to the molecule have also been identified. All of these acyclic compounds are unsaturated and may condense to form cyclic substances which, in turn, may remain as terpenic hydrocarbons or undergo further change to completely saturated or to aromatic compounds. All of these possibilities have been realized.

III. HEMITERPENE

A. ISOPRENE

Only a little work has been done on the thermal decomposition of isoprene. On the other hand, polymerization of isoprene, to which brief reference was made in a paper on olefins by Egloff, Schaad, and Lowry (44), has been the subject of quite extensive research. Indeed, since 1860 when Williams (192) established the fact that isoprene is not only a product of pyrolytic decomposition of rubber, but has the same empirical composition as rubber, a great amount of interest has been shown in the polymerization of isoprene to produce a commercially valuable synthetic rubber.

Catalytic decomposition

Staudinger, Endle, and Herold (158) studied the pyrolysis of isoprene at temperatures from 400°C. to over 800°C. In a typical run, isoprene vapors (349 g.) were passed through a quartz tube filled with coke and heated to about 750°C. The resulting gas contained 13.6 per cent unsaturated hydrocarbons, chiefly ethylene, 58–66.3 per cent methane, and 23.5–19.9 per cent hydrogen. From the tar were obtained 10 g. of benzene, 53 g. of toluene (boiling at 80–130°C.), 21 g. of naphthalene, 19 g. of α -methylnaphthalene, 15 g. of anthracene and phenanthrene, 18 g. of chrysene, 5 g. of a fraction boiling at 400–420°C., and 38 g. of tar and carbon.

At 400–500°C., isoprene was partially polymerized to higher unsaturated hydrocarbons, terpenic in nature, similar to those obtained as by-products in its polymerization to rubber. Some amylene and a small amount of gas, as well as unchanged isoprene, were recovered.

At 600–700°C. the transformation was almost complete. The mixture of unsaturated hydrocarbons formed, however, was no longer terpene-like, but rather resembled a crude petroleum. Gaseous products were also obtained in considerable amount, ethylene, propylene, and butadiene being identified.

Above 700°C., aromatic compounds begin to appear, and above 800°C. they are formed exclusively.

At 700°C., under 20 to 25 mm. pressure, almost half of the isoprene was unchanged. Highly unsaturated compounds were formed, but no tar. It was also found that under 15 mm. pressure isoprene could be distilled several times over a platinum spiral heated to bright redness without marked change.

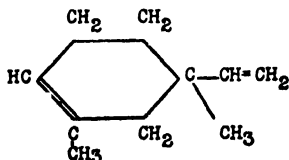
Polymerization under elevated temperatures

By heating isoprene in a sealed tube in an atmosphere of carbon dioxide for ten hours at 280–290°C., Bouchardat (22) obtained partial conversion to a product boiling at 167–171°C., which he called diisoprene (now called dipentene). In 1884 Tilden (171) confirmed this by heating isoprene to 250–280°C. in sealed tubes for twelve hours and obtained a yield of about 50 per cent dipentene.

Wallach (184) observed, as had Bouchardat and Tilden, that isoprene can be polymerized by the action of heat. He heated isoprene for several hours at 250–270°C., and obtained a product boiling at 180°C., which undoubtedly contained dipentene, for it yielded the characteristic dibromide.

Similarly, Harries (63) heated pure isoprene in a sealed tube at 300°C. A small portion polymerized to dipentene, but the chief product, besides the customary high-boiling oil, was an isomeric hydrocarbon, $C_{10}H_{16}$, which Wagner-Jauregg (182) later showed to be diprene.

Lebedev (94) reported that isoprene polymerized even below 0°C. The most suitable temperature, however, was 100–150°C., for at higher temperatures the reactions became complex. He heated the hydrocarbon in sealed tubes in this temperature range and distilled the product in a stream of hydrogen. The unaltered isoprene was taken off under ordinary pressure and a dimeride under 8 to 15 mm. pressure, while the polymeride remained behind. From experiments of different duration at 150°C., Lebedev (94) obtained the following amounts of polymer: 53 per cent in five hours, 79 per cent in fifteen hours, 90 per cent in thirty-eight hours. The dimeride fraction (95) consisted of two compounds, one of which was dipentene, b.p. 174–175°C., d_4^{20} 0.8454, and the other 1,3-dimethyl-3-vinyl-6-cyclohexene, b.p. 160–161°C., d_0^{20} 0.8331.



The higher the temperature, according to Lebedev (94), the greater is the ratio of dimeric to polymeric products, while at constant temperature this ratio remains the same regardless of the extent of transformation. The ratio is also affected by catalysts.

Gapon (52) studied the rate of polymerization of isoprene over the same temperature range in the absence of light. From experiments at 100°, 110°, 130°, and 150°C. he obtained, in all cases, four "primary" products:

dipentene, 1,3-dimethyl-3-vinyl-6-cyclohexene, and two polymers. His ideas of the mechanism of these changes have already been stated.

Ostromisslensky and Koshelev (114) reported that the polymerization of isoprene at a "higher temperature" gives normal isoprene caoutchouc. When, however, isoprene is heated to only 80 or 90°C. in a sealed vessel for three to five days, and its unchanged part removed by vaporization at 100°C., the residue after being steam-distilled yields a hydrocarbon, $C_{10}H_{16}$, which, on account of its resemblance to natural myrcene, Ostromisslensky called β -myrcene. It is a colorless mobile liquid, soluble in most organic solvents, boiling at 63.5°C. under 20 mm. pressure and, like natural caoutchouc, when treated with concentrated sulfur dioxide, gives a pre-

TABLE 2
Polymerization of isoprene

TEMPERATURE	TIME	OIL	RUBBER	MOLECULAR WEIGHT	RELATIVE VISCOSITY*
<i>degrees C.</i>		<i>per cent</i>	<i>per cent</i>		
85	97.5 hours	9.07	17.05	4589	4.62
	101 hours	7.9	16.25		
	900 hours		35.3	5715	8.20
145	5.25 hours	38.2	10.03	3291	3.14
	12.5 hours	54.7	15.56	3936	4.69
10	1 year	0.005	0.01		6.13†
Room temperature	4½ years	1.0	16.6	2312	13.4

* At 30°C. 1 cc. of solution containing approximately 0.68 g. per 20 cc. of benzene.

† At 30°C. 1 cc. of solution containing approximately 0.492 g. per 20 cc. of benzene.

cipitate "with double unions." Recently Wagner-Jauregg (182) has shown that β -myrcene is identical with diprene.

Whitby and Crozier (191), on the other hand, were unable to obtain β -myrcene from isoprene, even though Ostromisslensky's procedure was carefully followed. The only oily products isolated were cyclic dimers such as have been described by previous workers. They studied the effects of time and temperature on the polymerization of carefully purified isoprene, prepared from dipentene by use of the "isoprene lamp."

Their results were summarized in table 2.

Neither was there encountered any of the 1,3-dimethyl-3-vinyl-6-cyclohexane reported by Lebedev (94, 95). Except for the dimeric products mentioned by Harries (61), all of the dimers obtained from isoprene were clearly cyclic compounds. The sample which stood for four and

one-half years was found to contain dipentene, and it was believed by the experimenters that the material obtained in all of their studies was "preponderantly dipentene," though only oily bromine addition products could be obtained.

Polymerization by action of light

Wallach (186) observed that isoprene, exposed to light in a sealed tube for a long time, polymerized to a rubber-like mass. Some authors have claimed, however, that his isoprene, which was obtained from the dry distillation of rubber, may have contained an impurity, such as a small particle of rubber from the original material. This might have caused the re-formation of rubber, since evidence from other investigators (95) indicates that rubber itself catalyzes the polymerization of isoprene to caoutchouc. On the other hand, Harries (62) has shown that pure isoprene can be polymerized, by means of ultra-violet light, to a solid white substance which contains a small proportion of rubber-like material.

Spontaneous polymerization

The spontaneous polymerization of isoprene to rubber was observed by Tilden (170) in 1892. His isoprene, prepared by the thermal decomposition of turpentine, spontaneously became a dense syrup after standing for some time in bottles. There were several large masses of solid floating in this syrup, which proved to be "india rubber." Tilden accounted for the change by the hypothesis that "a small quantity of acetic or formic acid had been produced by the oxidizing action of the air and that the presence of these compounds had been the means of transforming the rest."

Two years after Tilden's paper was published, Weber (188) reported that 300 g. of isoprene, obtained from the dry distillation of rubber, were found after six months standing to be converted into a very viscous, treacly mass from which, by treatment with methyl alcohol, a solid, almost white, spongy substance could be separated. This substance, when dry, was identical with "india rubber." The by-products of the polymerization consisted of dipentene and polyterpenes.

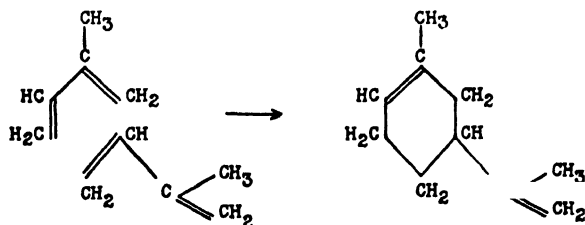
More recently Pickles (117) confirmed the observations of both Tilden and Weber. He found that isoprene acquired the consistency of a thick syrup after standing in closed bottles for two and a half years, mostly in the dark. However, he stated that the rubber, which was precipitated by alcohol, was not equal to para rubber in tenacity, but resembled the product of young rubber trees. "It undoubtedly contained rubber, as it yielded the characteristic nitroside and tetrabromide." These results and those of Weber would seem to indicate that Tilden's hypothesis involving

the formation of acetic and formic acid was unnecessary and possibly incorrect.

Harries (61) has gone even farther than Pickles, stating that comparative vulcanizing experiments indicated that the best specimens of isoprene caoutchouc are probably produced when polymerization takes place at the lowest possible temperature and without the addition of any foreign substance. "There were indications that isoprene caoutchouc contains an isomeric caoutchouc."

Aschan (5) has found that isoprene, kept in a sealed tube in an atmosphere of carbon dioxide in the dark for ten years, was only partially polymerized, 76 per cent of the unchanged isoprene remaining. From the dimeric compounds he obtained a small amount of diprene, b.p. 171–171.5°C., to which he assigned a formula based on a *p*-cymene structure. Later (6), he found that diprene and carvestrene yield identical dihydrochloride and dihydrobromide derivatives, but the hydrocarbons are not identical. Diprene, therefore, must have a *m*-cymene ring, but the double bonds are not located as in carvestrene.

Recently Wagner-Jauregg (182) has found (1) that the hydrocarbon ($C_{10}H_{16}$) obtained, together with caoutchouc and dipentene, by heating isoprene alone or with acetic acid, and regarded by Harries (61) as 2,6-dimethyl-1,5,7-octatriene, contains only two double linkages and when hydrogenated in the presence of platinum oxide, produces *m*-menthane; (2) that a *m*-menthadiene, obtained by autopolymerization of isoprene and described by Aschan (6) as diprene, is identical with Harries' hydrocarbon; and (3) that β -myrcene, obtained by Ostromisslensky (114) by heating isoprene at 80–90°C. for several days, is identical with diprene and is the sole dimeride of isoprene formed under these conditions. Diprene is not considered to be a pure compound, but a mixture of similar compounds which boil within a temperature interval of 4°C. The position of the double bonds in diprene has not yet been proven, but the reaction may be represented as follows:



Polymerization under high pressure

Isoprene is partially polymerized when subjected to a pressure of 9000 atmospheres for twenty-four hours. Bridgeman and Conant (27) have

TABLE 3
Polymerization of isoprene under high pressures

PRESSURE	TIME	EXTENT OF POLYMERIZATION
<i>atmospheres</i>	<i>hours</i>	<i>per cent</i>
12,000	50	Practically complete
9,000	24	40-45
6,000	48	10
3,000	68	Only a trace

TABLE 4
Polymerization of isoprene after standing

NO.	DAYS STANDING BEFORE POLYMERIZATION	PER CENT POLYMERIZATION
1	1	34
2	3	64
3	7	86
4	11	Apparently same as No. 3
5	9	88
6	9 (sample redistilled)	25

TABLE 5
Polymerization of two lots of isoprene after standing for eight days
Pressure, 12,000 atmospheres; temperature, 23-25°C.

TIME	PER CENT POLYMERIZED	REACTION CONSTANT $K \times 10^2$
Lot No. 1		
<i>hours</i>		
5	27	6.3
5	33	8.0
5	35	8.6
16	83	11.2
20	87	10.2
Average.....		8.9
Lot No. 2		
5	11	2.3
20	61	4.7
23	66	4.7
23	65	4.6
Average.....		4.1

found that the product formed on such treatment is a soft jelly-like solid which, on standing for twenty-four hours in the open, lost 60 per cent of its weight by evaporation and shrank to a denser rubber-like solid which was yellow but transparent.

On the assumption that the loss in weight by evaporation on standing represents the unpolymerized isoprene, the results of Bridgeman and Conant's work at various pressures may be expressed as in table 3.

Since the publication of the above preliminary paper, Conant and Tongberg (34) have attempted to measure the effect of pressure and temperature on the rate of polymerization of isoprene, but were severely handicapped by the difficulty of preparing uniform samples of isoprene. The use of freshly distilled material did not solve the difficulty, as varying amounts of peroxides were formed in irregular fashion and these were found to play an important part in the acceleration of the polymerization. The most consistent results were obtained with samples of isoprene which had been allowed to stand at least seven days at 2°C. in nitrogen or air, while standing for a longer time only slightly altered the tendency to polymerize. The data in table 4 serve to illustrate the above variations for tests of twenty hours duration.

The most significant data were obtained with two different lots of isoprene which had stood for at least eight days; they are shown in table 5.

The reaction velocity constants were calculated according to the first-order equation in order to have a means of comparing the extent of the reaction at different times, although it is presumably of high order.

The product obtained from these experiments was a transparent, colorless rubbery solid.²

In a study of the effect of pressure on the rate of polymerization, Tamman and Pape (168) state that the polymerization of isoprene follows the unimolecular law and suggest that the molecules undergo some change before union, the rate of this reaction determining the speed of the process as a whole. The velocity increases with increase in pressure much more rapidly than in other reactions occurring in liquids.

Polymerization catalyzed by various reagents

(1) *Peroxides.* Many patents for the use of peroxides as catalysts in the polymerization of isoprene have been issued, but the effect of such catalysts seems not to have been studied until recently.

Conant and Tongberg (34) stated that peroxide catalysts play a very important part in the acceleration of polymerization, but are not essential to the process. They found that the catalyst which gave the most con-

² Conant and Tongberg give a detailed discussion of the nature of the products obtained under different conditions.

sistent results was a sample of pinene which had been shaken with oxygen for four or five hours and which was used from time to time without further treatment. The results are summarized in table 6, the first-order reaction constants being given as a rough measure of the rate of polymerization.

TABLE 6
Polymerization of isoprene catalyzed by pinene
Pressure, 12,000 atmospheres; temperature, 23–25°C.

AMOUNT OF CATALYST	TIME	PER CENT POLYMERIZED	REACTION CONSTANT $K \times 10^3$
<i>per cent</i>	<i>hours</i>		
0.1	4.5	83	39.3
0.1	4.5	63	22.1
Average.....			30.7
0.04	4.5	28	7.3
0.04	4.5	41	11.7
0.04	4.5	63	22.1
Average.....			13.7
0.01	4.5	38	10.6
0.01	4.5	12	2.8
0.01	16.0	54	4.8
Average.....			6.1
0.002	15.75	55	5.1
0.002	15.75	55	5.1
Average.....			5.1
0.001	4.5	7	1.6
0.001	4.5	12	2.8
0.001	15.0	24	1.8
Average.....			2.1

Many experiments were carried out in an attempt to obtain sufficient information for the determination of the pressure and temperature coefficients of the rate of polymerization. "A comparison of these coefficients shows that, at higher pressures and room temperature, a change of 15°C. is about equivalent to 3000 atmospheres pressure, with regard to the effect on the reaction rate. Over a wider range it is estimated that raising the pressure from 2000 atmospheres to 12,000 atmospheres increases the rate about one hundred-fold; this increase could also be obtained by raising

the temperature from about 20 to 60°C. If the temperature and pressure coefficients of the polymerization of isoprene are typical, it is clear that the mere acceleration of the reaction is more readily accomplished by raising the temperature than by increasing the pressure. However, there must be many cases (and the polymerization of isoprene is probably one) where the nature of the products differs according to whether they are formed at high pressures or elevated temperatures."

More recently Conant and Peterson (33) have come to the conclusion that peroxide catalysis is essential to the pressure polymerization of isoprene, and present the following evidence. "Peroxides and ozonides have a strong positive catalytic action. Freshly distilled isoprene polymerizes at a rate only one-fifth to one-tenth of that of isoprene which has stood in the air for some days. This increased tendency to polymerize on standing is almost certainly due to the formation of peroxides from the dissolved oxygen. If peroxides (or dissolved oxygen which will form a peroxide) are essential to the polymerization, we must assume that when the isoprene was distilled in nitrogen some trace of oxygen or volatile peroxides was in the distillate. We have now strong evidence for this assumption, since we have found that by adding hexaphenylethane (which reacts rapidly with oxygen) to isoprene in nitrogen and distilling, the rate of polymerization of the distillate is reduced tenfold. The material thus prepared still polymerizes under pressure (14 per cent at 12,000 atmospheres in forty-eight hours); it can be argued that this represents the uncatalyzed reaction, but it seems equally probable that traces of oxygen or peroxide are still present adsorbed to the glass."

In view of these facts, they suggest "that the mechanism is a series of chain reactions in the liquid initiated by the spontaneous decomposition from time to time of the peroxide. The accelerating effect of great pressures is due, according to our theory, to the orientation of the molecules of the isoprene into a more compact bundle in which longer reaction chains would be propagated by the spontaneous decomposition of a single peroxide molecule. It seems quite certain that as the volume of a liquid is diminished by the application of pressure, a definite orientation of the molecules is approached and we assume that this orientation is very similar to that existing in the polymer itself. It seems reasonable to suppose that the spontaneous decomposition of a peroxide molecule would be more effective in producing long reaction chains, the less the random motion of the molecules and the more compact and oriented they were assembled. We imagine that as each molecule becomes in turn activated by the energy originally coming from the peroxide, it unites with its neighbor, which in turn becomes active by virtue of the exothermic nature of the polymerization process. The pressure polymerization is thus to be thought of as

a chain reaction in which the energy is passed on in a chain and all the reacting molecules actually unite. The accelerating effect of temperature is easily explained as being due to the more frequent initiation of peroxide decompositions and hence of reaction chains."

Staudinger and Lautenschlager (161) have determined the rate of polymerization of isoprene by heating 10 g. at 80°C. in the presence of carbon dioxide or oxygen for four days and removing all of the material volatile below 80°C. under vacuum. The per cent of polymerization and of oxidation is shown in table 7.

Addition of peroxides causes polymerization to occur more rapidly than in carbon dioxide, but not so quickly as in oxygen. Therefore, it is concluded that the peroxides are not the actual catalysts and that primary peroxides with more pronounced accelerating action are formed during autoxidation.

TABLE 7
Polymerization of isoprene

TIME	AUTOXIDATION*	POLYMERIZATION IN OXYGEN	POLYMERIZATION IN CARBON DIOXIDE
<i>days</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
1	0	10	5
2	0	13	6
3	0	18	7
4	3	23	9

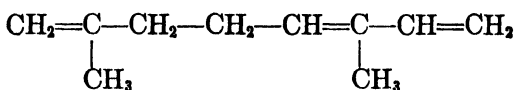
* This calculation is based on the assumption that one molecule of hydrocarbon absorbs only one molecule of oxygen.

(2) *Caoutchouc*. As mentioned above, the polymerization of isoprene is aided by the presence of caoutchouc or caoutchouc-like material. Lebedev and Skavronsky (95) report that when a small piece of caoutchouc is sealed with 35 g. of isoprene, it gradually grows and in three years the polymerization is complete. If no polymer is originally introduced, the liquid becomes very viscous, the first insoluble polymer is noticed only toward the end of the second year, and at the end of three years much liquid is still left.

(3) *Acids*. In 1879 Bouchardat (24) found that the distillation of the hydrochlorides of isoprene (formed by allowing isoprene to stand in hydrochloric acid for twenty-five days) yielded a solid residue with the elasticity and other properties of rubber. It contained little more than 1 per cent of chlorine. This work was confirmed by Tilden (171) in 1884. However, there has been controversy over the question of the formation of rubber from isoprene in the presence of hydrochloric acid. Pond (118) has reviewed this controversy and attempted to repeat the work of Bouchardat and Tilden but without success.

In 1910 Harries (64) reported the discovery that isoprene can be converted to rubber by heating it with glacial acetic acid to about 100°C. in a sealed tube. This rubber was identical with "india rubber" in physical as well as chemical properties. He stated that unless the various conditions are maintained constant, all sorts of viscous oils, resins, etc., are obtained, but he did not report the optimum conditions. A year later (61) he stated that when isoprene is converted to isoprene caoutchouc by heating (on a water bath) under pressure with an equal volume of glacial acetic acid for eight days the yield varied widely, but was little if at all affected by marked variation in the proportion of acetic acid or by changes in the temperature between 95 and 120°C.

As a by-product of this process Harries obtained a hydrocarbon, $C_{10}H_{16}$, which he considered to have the following formula.



As has already been shown, Wagner-Jauregg (182) has repeated Harries' work and found that this terpene is identical with diprene.

More recently he (183) obtained a hydrocarbon, to which he gave the formula $C_{16}H_{24}$, by treating isoprene with an excess of glacial acetic acid, containing a little concentrated sulfuric acid, for three days at room temperature. Various terpene alcohols were produced together with the hydrocarbon, when the reaction mixture was hydrolyzed. Similar treatment with a mixture of glacial acetic acid and a little dilute sulfuric acid yielded the same hydrocarbon, together with a mixture of terpene alcohols and ethers, without subsequent hydrolysis.

Hydration of ethylenic bonds in the molecules produced by the polymerization of isoprene, either simultaneously with or subsequently to the polymerization, was thought to be the source of the alcohols and ethers which were found.

The hydrocarbon appeared to be a monocyclic compound with three double bonds, isomeric with bisabolene and zingiberene, but gave no crystalline hydrogen chloride addition product. It added three moles of hydrogen, catalytically.

Refluxed with 98 per cent formic acid, there resulted a product thought to be a bicyclic hydrocarbon of the caryophyllene group, containing two double bonds. Similar treatment of bisabolene and zingiberene yields bicyclic hydrocarbons of the cadinene group.

(4) *Alkali metals.* Harries (61) prepared a so-called sodium-caoutchouc from the polymerization of isoprene with 0.4 per cent sodium at 60°C. Fifty hours heating produced an almost quantitative yield of caoutchouc.

It is interesting to note that Harries claimed that his caoutchouc had properties "identical" with those of natural rubber save that it yielded different ozonization products.

Aschan (8) claims to have discovered the condensing action of sodium on isoprene independently of, and simultaneously with, Harries. He obtained, from crude isoprene and sodium, a product insoluble in alcohol but soluble in ether, which he termed "semi-caoutchouc," and which could be vulcanized. Pure isoprene, heated alone for thirteen days, was less completely polymerized than in three days in the presence of sodium.

Midgley and Henne (104) have found that isoprene is dimerized when placed in contact with metallic potassium chips and ethyl alcohol added at a rate just sufficient to give a moderate evolution of hydrogen at the surface of the metal. The light yellow oil which resulted, proved to be a mixture of 2,6-, 2,7-, and 3,6-dimethyl-2,6-octadienes. These isomers are the dihydro dimers of isoprene resulting from a junction at the 1,4-, the 4,4- and the 1,1-carbon atoms, respectively, and the addition of hydrogen at the 1,8-positions of the dimer. No trace of a cyclic compound could be detected.

(5) *Metallic chlorides.* High molecular weight polymers, said to be isomeric with rubber, have been produced by catalytic action at room temperature. Whitby and Crozier (191) treated 0.5 cc. portions of pure isoprene with inorganic halides with the following results:

(a) Stannic chloride.—Polymerization was complete in three hours, yielding a clear, soft, amber colored, non-elastic mass, which when warmed showed elastic properties if squeezed, and which swelled but did not dissolve in benzene. The addition of alcohol converted this substance to a white powder.

(b) Antimony pentachloride.—If the catalyst was added undiluted, there resulted a violent reaction, producing a pitch. If diluted with an organic solvent, or used at the temperature of solid carbon dioxide, the product resembled that produced by stannic chloride at room temperature.

(c) Antimony trichloride.—At room temperature, violent reaction, with charring, resulted. At the temperature of solid carbon dioxide the product was similar to that from stannic chloride.

(d) Ferric chloride.—Only a slight effect after two days.

(e) Ferric bromide.—A brown, weak gel after twelve hours.

(f) Aluminum chloride.—Complete polymerization after twenty-four hours to a yellow flaky mass, only slightly soluble in benzene.

(g) Thorium bromide and thorium chloride.—Little or no action in dilute solution after twenty-four hours. The addition of alcohol precipitated small amounts of the powdery polymer.

Similar products were obtained by treating 3 per cent solutions of rubber in benzene with the same catalysts, and then with alcohol.

More recently Wagner-Jauregg (183) treated isoprene with titanium tetrachloride at room temperature and obtained a similar polymer. It was a slightly yellow, amorphous substance which first softened and then melted with decomposition when heated. It was soluble in benzene, partially so in ether and pyridine, and was precipitated from these solvents by alcohol. Its molecular weight in benzene was about 2800.

This polymer resembled that obtained from Dammar resin $(C_8H_8)_x$, the molecular weight of which averages 2800 to 3000, and which possesses similar solubilities. It was supposed that they belong to the same class of substances.

On being heated with selenium, dehydrogenation occurred, yielding 1,2,5-trimethylnaphthalene, obtained by Ruzicka (133) by the selenium dehydrogenation of certain triterpenes and sapogenins.

At a temperature of 110°C ., antimony trichloride was found by Euler and Ahlström (46) to give with isoprene an amorphous product which did not melt at 300°C . The authors supposed it to be a very high condensation product of isoprene, although the carbon content analyzed about 3 per cent low. At room temperature an amorphous product having the formula $C_{10}H_{16} \cdot 2SbCl_3$ resulted.

The same authors found that when isoprene was heated with azobenzene at 100 – 120°C . some dipentene appeared among the reaction products.

Heating with amyl nitrite at 130 – 140°C . produced a dark rubbery mass containing no nitrogen.

Aschan (9) has shown that in the presence of aluminum chloride isoprene condenses with itself and also with other hydrocarbons containing an ethylenic linkage, such as amylene, trimethylethylene, pinene, camphene, isopinene, dipentene, and sylvestrene, yielding amorphous compounds of high molecular weight which do not possess the physical properties of caoutchouc. The time necessary for the completion of the condensation, when "commercial" isoprene (4) is used, is only a few minutes. The product can always be separated into two components, both unsaturated solids, one of which is completely insoluble in all solvents, while the other dissolves in most organic media with the exception of alcohol. Experiments with mixtures of isoprene and amylene showed that, practically, only the isoprene was acted on if the proportion of amylene was small and the test cautiously performed. Oily substances, which are possibly synthetic hydrocarbons of the sesqui-, di-, and poly-terpene series, are obtained as by-products of these condensations.

Recently Thomas and Carmody (169) have published the results of a similar study of isoprene and pentene-2. These authors found that the insoluble substance, $(C_8H_8)_x$, was converted at 300°C . to a dark oil which solidified on cooling to a dark transparent resin, soluble in hydrocarbon

and chlorinated hydrocarbon solvents. The quantity of this polymer produced was an inverse function of the amount of pentene-2 present.

The soluble polymer varied in physical state from a viscous oil to a hard resin, depending on the amount of pentene-2 present and the subsequent treatment. It consisted of a mixture of higher oils and a hydrocarbon resin. The hardness and molecular weight were inverse functions of the amount of pentene-2 added, the latter varying from 845 to 1240. As the lower oils were removed, the formula approached $(C_8H_8)_x$.

It was found that any solvent in which isoprene and aluminum chloride were mutually soluble caused formation of the soluble polymer. Thus nitrobenzene and ethyl acetate could be used. With the former, in which aluminum chloride is completely soluble, only the soluble polymer was formed, while with the latter, in which the chloride is less soluble, some of the insoluble polymer was produced, the quantity being less with increasing quantities of the ester.

Dry hydrogen chloride, bubbled through isoprene containing aluminum chloride, caused a violent reaction, producing both polymers because the hydrochloride of isoprene formed a complex with aluminum chloride in which both isoprene and the salt were soluble to some extent.

There was only a slow polymerization to the insoluble form, when pure isoprene and aluminum chloride were allowed to stand at room temperature. Thomas and Carmody supposed that this polymer had a high molecular weight, while the soluble form had a much lower molecular weight, the actual value of which depended on the amount of mutual solvent present.

The formation of the two polymers was explained by assuming that in the absence of a mutual solvent only a small catalytic surface was exposed, and that the isoprene molecules could only continue to build up on the comparatively few nuclei started at that surface. In the presence of a mutual solvent, however, the dissolved catalyst presented a very much larger surface, many more polymeric molecules formed, and therefore the formation of large, insoluble molecules or aggregates was prevented because of the relatively fewer isoprene molecules available for polymerization at a given point.

Böeseken and Adler (20) have found that isoprene, if brought into contact with aluminum chloride in benzene solution, is converted to a mixture of polyisoprenes which have no resemblance to caoutchouc.

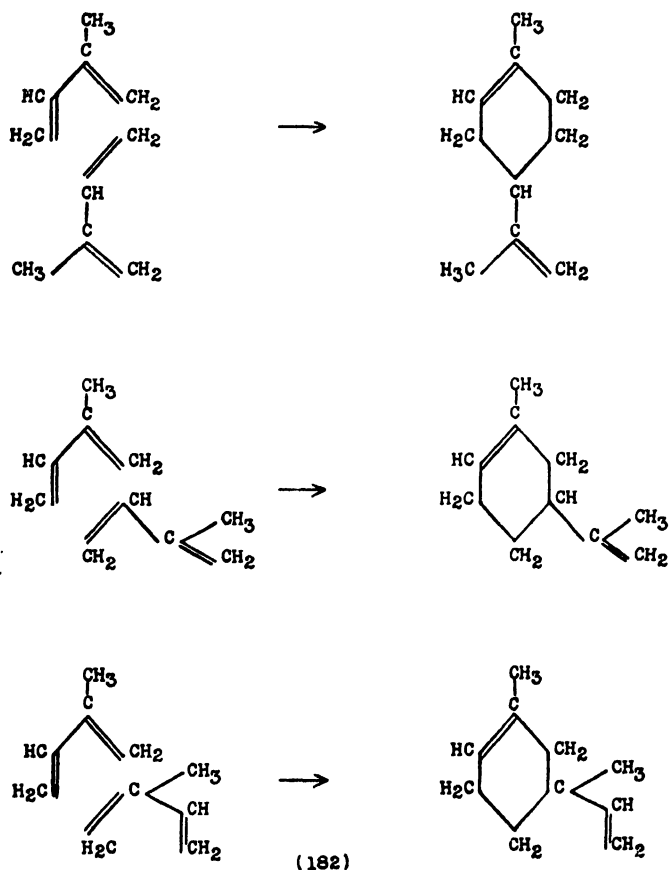
(6) *Aluminum-mercury couple.* At about the same time that Aschan's work on the catalytic effect of aluminum chloride appeared, Böeseken and Nooduijn (21) reported the polymerization of isoprene in benzene solution under the influence of an aluminum-mercury couple. This catalyst was prepared by pouring 0.2 g. of powdered aluminum into a dry benzene

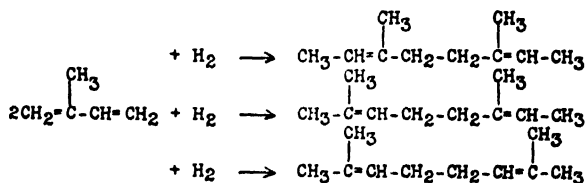
solution of 3 g. of mercuric chloride and warming gently. After cooling, 10 g. of isoprene in 40 cc. of benzene was added, the mixture warmed half an hour on the water bath, and allowed to stand twenty-four hours.

Like Aschan, they obtained two kinds of products, both unsaturated polymers of high molecular weight, which were only slightly viscous and could not be vulcanized. One of the products was soluble in benzene, ether, chloroform, etc., while the other was nearly insoluble.

(7) *Radon*. Heisig (73) studied the action of radon on isoprene, and pointed out that a rubber-like product might have been expected, but that the material obtained was a very viscous light-colored liquid which had the same general appearance as the rubber left after the evaporation of the "solvent" from rubber cement. The indications were that hydrogen and methane were formed.

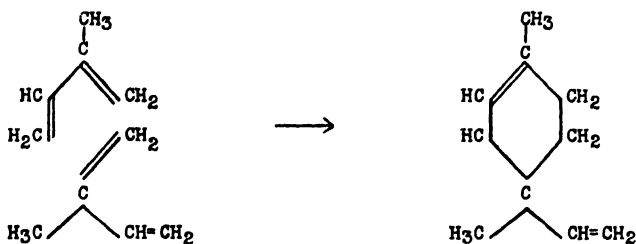
The present state of our knowledge of the manner in which isoprene may be dimerized is summarized by the following equations.





(104)

The reaction represented below seems reasonable, although it has not been realized as yet.



The patent literature on the polymerization of isoprene is too voluminous to include in this paper. However, it reports that polymerization of

TABLE 8
Pyrolysis of isoprene
 (Quartz tube with coke as catalyst (158))

TEMPERATURE	PRODUCTS
<i>degrees C.</i>	
400-450	Isoprene, terpenes, amylene, a little gas
600-700	Unsaturated mixture resembling crude petroleum, ethylene, propylene, butadiene
700	Aromatics begin to appear
750	Gaseous unsaturated hydrocarbons, ethylene, methane, hydrogen, benzene, toluene, naphthalene, α -methylnaphthalene, anthracene, phenanthrene, chrysene, tar, carbon
800	100 per cent aromatics
700 (under 20 mm. pressure)	50 per cent isoprene, gases, unsaturated compounds (no tar)

isoprene may be hastened by heat, light, radon, silent electric discharge, and many chemical reagents. The products obtained are terpenes and rubber or rubber-like materials.

The results of investigations on isoprene reported in this paper, are summarized in tables 8 and 9.

TABLE 9
Polymerization of isoprene

REFERENCE NO.	TIME	TEMPERATURE	PRODUCTS	REMARKS
		<i>degrees C.</i>		
(22)	10 hours	280-290	Diisoprene	Sealed tube with atmosphere of CO ₂
(171)	12 hours	250-280	Dipentene	Sealed tube
(184)	"Several hours"	250-270	Dipentene	Sealed tube
(63)	—	300	Dipentene, and an isomeric substance	
(94)	—	100-150	Dipentene, 1,3-dimethyl-3-ethylenyl-6-cyclohexene	Heated in sealed tube and then distilled in stream of hydrogen
(114)	3-5 days	80-90	(β -Myrcene)	Sealed tube
(53)	—	100-150	Dipentene, 1,3-dimethyl-3-vinyl-6-cyclohexene, two polymers	Absence of light
(186)	—	Room temperature	Caoutchouc-like mass	Presence of light
(62)	—	Room temperature	Rubber-like material, and solid white substance	Ultra-violet light
(170)	—	Room temperature	Dense syrup, rubber-like solid	
(188)	6 months	Room temperature	Viscous mass	
(117)	2½ years	Room temperature	Rubber-like product	Absence of light
(5)	10 years	Room temperature	Diprene	Absence of light
(27)	20 hours	Room temperature	Rubber-like product	High pressure
(95)	3 years	Room temperature	Complete polymerization	Small piece of rubber added
(95)	3 years	Room temperature	Liquid polymer	
(24)	25 days	Room temperature	Elastic solid residuc, and hydrochlorides of isoprene	Products obtained on distillation after standing with HCl
(171)			—	Confirmation of HCl action above
(64)	8 days	100	Rubber, viscous oils, resins, C ₁₀ H ₁₆ oil	Heated in sealed tube with glacial acetic acid

TABLE 9—Continued

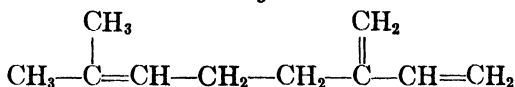
REFERENCE NO.	TIME	TEMPERATURE	PRODUCTS	REMARKS
		<i>degrees C.</i>		
(61)	50 hours	60	Caoutchouc	Almost quantitative yield. Sodium used as catalyst
(8)	3 days	"Heat"	Caoutchouc	Crude isoprene catalyzed by sodium
(104)	—	—	2,6-, 2,7-, and 3,6-dimethyl-2,6-octadiene	Sodium and ethyl alcohol
(4)	Few minutes	—	Two unsaturated solids, oily by-products	"Commercial" isoprene catalyzed by AlCl_3
(20)	—	—	Polyisoprenes	AlCl_3 in benzene solution
(21)	24 hours	100 for $\frac{1}{2}$ hour then room temperature	Products same as above	Benzene solution with or without H_2 atmosphere in presence of Al-Hg couple
(73)	—	—	Viscous liquid, hydrogen (?), methane (?)	Radon
(191)	5 hours to 4½ years	Room temperature to 145	Oil and rubber, dipentene	No β -myrcene or 1,3-dimethyl-3-vinyl-6-cyclohexane
(182)	3 days	Room temperature	$\text{C}_{18}\text{H}_{24}$ hydrocarbon	Acetic-sulfuric acid added
(191)	3 hours	Room temperature	High molecular weight polymer	SnCl_4 added
	—	—80 or room temperature, if diluted	High molecular weight polymer	SbCl_5 added
	—	—80 or room temperature, if diluted	High molecular weight polymer	SbCl_5 added
	2 days	Room temperature	Slight effect	FeCl_3 added
	12 hours	Room temperature	Weak gel	FeBr_3 added
	24 hours	Room temperature	Flaky polymer	AlCl_3 added
		Room temperature	Little or no action	ThBr_4 and ThCl_4 added

TABLE 9—*Concluded*

REFERENCE NO.	TIME	TEMPERATURE	PRODUCTS	REMARKS
		<i>degrees C.</i>		
(182)	—	Room temperature	High amorphous polymer	TiCl ₄ added
(46)	—	110	Amorphous polymer	SbCl ₅ added
		100–120	Dipentene and other products	Azobenzene added
		130–140	Rubbery polymer	Amyl nitrite added
(169)	—	Room temperature	High molecular weight insoluble polymer, low molecular weight soluble polymer	AlCl ₃ and pentene-2 added

IV. MONOTERPENES

A. ACYCLIC

1. *Myrcene*

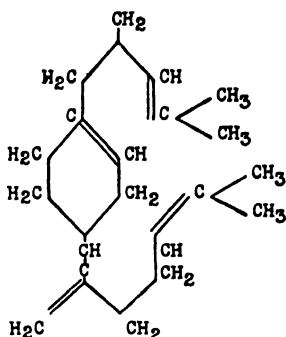
Thermal decomposition. As has already been stated, the formula of myrcene indicates that its reactions under the influence of heat should be similar to those of isoprene. However, the decomposition products of myrcene have not been studied to as great an extent.

When myrcene was subjected to pyrolytic decomposition using a glowing platinum wire and brass jacket, Prodrom (120) found that the product contained 3.6 per cent gases, 15.9 per cent of material boiling between -80° and $25^\circ\text{C}.$, 39 per cent crude isoprene, 26.8 per cent of liquids boiling above $45^\circ\text{C}.$, and 14.6 per cent of residue. A 60 to 70 per cent yield of isoprene from the decomposition of myrcene in the presence of benzene vapors has been reported by Ostromisslensky (113).

Polymerization. Like the thermal decomposition, the polymerization of myrcene has not been studied in great detail. Harries (63) reported that myrcene is polymerized to a thick greenish yellow oil when heated for four hours in a sealed tube at $300^\circ\text{C}.$ On fractionation of the product under 13 mm. pressure, three fractions were obtained: (1) unchanged or "cyclomyrcene" boiling at 50 – $100^\circ\text{C}.$, (2) dimyrcene ($\text{C}_{20}\text{H}_{32}$), boiling at 160 – $200^\circ\text{C}.$, and (3) a residue of polymyrcene ($\text{C}_{40}\text{H}_{64}$).

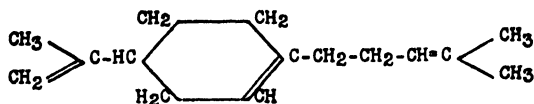
Similar to the work of Harries was that of Semmler and Jonas (152), who heated myrcene for four hours in a sealed tube at 250 – $260^\circ\text{C}.$ and

fractionated the product. The fraction which corresponded to Harries dimyrcene contained 50 per cent α -camphorene, and other diterpenes some of which were probably bicyclic. The formula of α -camphorene as suggested by Ruzicka and Stoll (132) is as follows:



Prodrom (120) found that purified myrcene heated for three weeks at 100°C . under pressure was converted to a transparent viscous oil, which on fractionation under 1 mm. pressure gave products with boiling ranges of $50\text{--}53^{\circ}$, $170\text{--}176^{\circ}$, and above 269°C ., respectively.

When heated at 225°C . for three and one-half hours, a mixture of 20 g. of myrcene and 10 g. of isoprene (152) yielded the following fractions upon distillation under 8 mm. pressure: (1) dipentene, boiling range $52\text{--}65^{\circ}\text{C}$.; (2) cycloisoprene-myrcene, boiling range $120\text{--}150^{\circ}\text{C}$.; (3) oil of boiling range $175\text{--}195^{\circ}\text{C}$.; and (4) residue. The following formula for cycloisoprene-myrcene has been suggested by Ruzicka and Bosch (126).



Concerning the rate of polymerization of myrcene, Lebedev (94) has found that at 150°C . myrcene is polymerized to the extent of 53 per cent in four and one-half hours, 68 per cent in thirteen and one-half hours, 78 per cent in one hundred and fifteen hours, and 82.5 per cent in two hundred and eighty-eight hours.

Staudinger and Lautenschlager (161) reported that at 80°C . myrcene undergoes oxidation and polymerization to the extent shown in table 10.

Gapon (54) considers that myrcene is most likely a mixture of two isomers, and that on activation three active forms will be produced, thus giving rise to two dimers and two polymers. The kinetics of the reaction were studied and it was found that two processes occurred, a polymeri-

zation and an isomerization. Gapon determined the rates of the two reactions at 150°C.

TABLE 10

Myrcene

TIME	AUTOXIDATION	POLYMERIZATION IN OXYGEN	POLYMERIZATION IN CARBON DIOXIDE
<i>days</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
1	62	20	10
2	78	32	14
3	82	42	17
4	90	50	22

TABLE 11

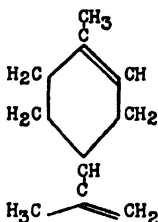
Myrcene

REFER- ENCE NO.	TIME	TEMPERATURE	PRODUCTS	REMARKS
	<i>hours</i>	<i>degrees C.</i>		
(120)	—	Glowing platinum wire	Gases, crude isoprene, liquid boiling above 45°, residue	Brass jacket
(113)	—	—	Isoprene	Benzene vapor used as diluent
(63)	4	300	Unchanged or cyclomyr- cene, dimyrcene (C ₂₀ H ₃₂), residue (C ₁₀ H ₁₄)	
(152)	4	250-260	Same as above with addi- tion of α -camphorene	Sealed tube
	3.5	225	Dipentene, cycloisoprene- myrcene, unknown boil- ing at 175-195°, residue	Myrcene and isoprene heated in sealed tube
(120)	3 weeks	100	Unknowns of following boil- ing point: 50-53° at 1 mm. pressure, 170-176° at 1 mm. pressure, above 269°	Purified myrcene heated under pres- sure
(94)	4.5 13.5 115 288	150	53 per cent polymer, 68 per cent polymer, 78 per cent polymer, 82.5 per cent polymer	

Since β -myrcene has been found to be identical with diprene, its behavior is discussed under the latter heading.

Table 11 summarizes the results of investigations of the polymerization and depolymerization of myrcene.

B. MONOCYCLIC TERPENES

1. Limonene (*dl*-limonene = dipentene)

Non-catalytic decomposition. In spite of the wide distribution of *d*- and *l*-limonene and the *dl* (racemic) form, dipentene, there are comparatively few detailed accounts of their pyrolysis.

In 1902 Harries (63) reported that both limonene and dipentene remain for the most part unchanged on being heated for four hours in a sealed tube at 300°C.

Several years later Harries and Gottl b (65) developed the "isoprene lamp" for the decomposition of terpenes to isoprene. This consisted of an electrically heated platinum filament suspended in the upper portion of a flask equipped with a reflux condenser maintained at 50°C. Thus the isoprene and low-boiling products were continuously removed, and the higher boiling terpenes remained in the flask. Using the isoprene lamp Harries and Gottl b obtained 30 to 50 per cent of isoprene from commercial carvene (largely dipentene), depending upon the dipentene content.

Some doubt was cast on Harries' work when Herty and Graham (77) obtained, with the isoprene lamp, only a 12 per cent yield of isoprene from the volatile oil of *Pinus Serotina*, an oil which had been found by Herty and Dickson (76) to be particularly rich in limonene. Furthermore, Mahood (99) has pointed out that wood turpentine, which contains a considerable amount of limonene, might be expected to give a larger yield of isoprene than gum turpentine, which is largely pinene. His results, however, did not confirm this supposition.

In order to get a little more direct evidence of the yields of isoprene available from pinene and limonene, Mahood (99) carried out experiments in which turpentine was treated so as to convert the pinene into limonene before cracking. Wallach (184) had observed previously that pinene is converted to limonene by prolonged heating at 250–270°C. Mahood ran several experiments in which the vapors of gum turpentine were passed through an iron tube heated to 250–270°C. for two to twenty hours. The original turpentine, which consisted largely of pinene, was converted

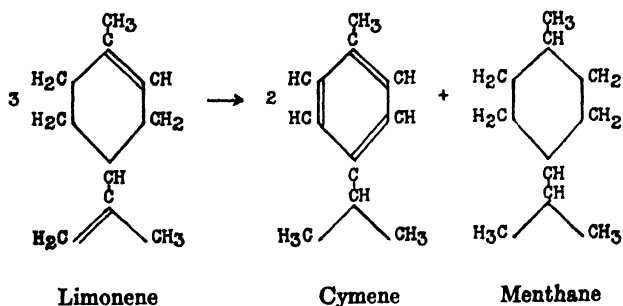
to a more complex and higher boiling mixture of which limonene was one of the chief constituents. There was, however, no appreciable increase in the yield of isoprene upon cracking this product by passing it through a Pyrex glass tube at 450°C.

On the other hand, Supniewsky (167), in a more recent paper reported that he obtained 100 g. of pure isoprene and 80 g. of a mixture containing some isoprene from 300 g. of limonene, the isoprene lamp being the means of conversion.

Staudinger and Klever (160) obtained a 60 per cent yield of isoprene by passing the vapors of dipentene in high dilution with nitrogen over a hot platinum coil at a pressure of 20–30 mm. When the pressure was reduced to 2–3 mm., even larger yields of isoprene were obtained. In both cases they obtained a small quantity of gaseous hydrocarbons of the olefin and acetylene series and of liquid hydrocarbons boiling from 100–150°C. Hardly any higher boiling compounds were produced.

Ostromisslensky (113) has stated that Staudinger and Klever's results were not due to the dilution of the limonene vapor but to the high temperature at which this vapor is formed. He states also that "good results" are obtained when limonene is mixed with benzene, toluene, xylene or light petroleum.

Catalytic decomposition. In the work in which the isoprene lamp was used, the glowing platinum wire was considered simply as a source of heat, and no mention was made of any catalytic action. Palladinized asbestos at 180–185°C., however, was found by Zelinsky (196) to exercise a non-reversible catalytic effect on limonene. The limonene, b.p. 166.5–177.5°C., was converted after a single passage over the catalyst into about 66 per cent *p*-cymene and 33 per cent menthane. The same transformation was effected at 130°C. under 120 mm. pressure.



Komatsu and Kurata (90) have found that *d*-limonene passed over a reduced copper catalyst at 280–300°C. yielded cymene quantitatively. However, if the temperature was lowered to 200°C. and the limonene

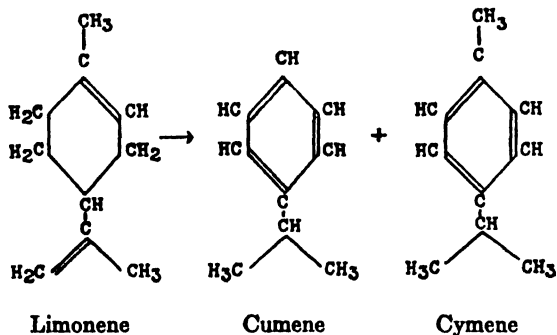
passed over the copper at the same rate, both cymene and menthane were found in the products.

The action of nickel and copper catalysts on limonene was found by Treibs and Schmidt (172) to be analogous to that of Zelinsky's palladium-asbestos catalyst, yielding cymene and menthane as products.

Decomposition in glow discharge. The decomposition of limonene and dipentene in a glow discharge has been studied by Linder and Davis (96). As might be expected, the rate of decomposition, measured by gas production, is about the same in both cases. The products obtained from dipentene were hydrogen, gaseous acetylenes, olefins and paraffins, and hexaethylbenzene. The gases from limonene were similar to those from dipentene but the solid which was reported was *o*-diphenylbenzene.

Catalytic hydrogenation. Some very interesting work has been done on the hydrogenation of limonene and dipentene at elevated temperatures. Sabatier and Senderens (138) have found that limonene and hydrogen passed over a nickel catalyst at 180°C. yield hydrocymene (*p*-menthane) and a small quantity of decomposition products. The same authors (139) reported that the hydrogenation of limonene over copper at 190°C. changes limonene to *p*-1-menthene. Somewhat later, Vavon (180) studied the stepwise hydrogenation of limonene using platinum black as catalyst and found that *p*-1-menthene can be obtained by stopping the hydrogenation after one mole of hydrogen has been absorbed, while *p*-menthane is obtained if the reaction is allowed to go to completion.

At somewhat higher temperatures, 350–360°C., Sabatier and Gaudion (136) found that the vapors of limonene carried along by hydrogen and directed on a column of nickel yielded for the most part cymene mixed with cumene:



Only a small amount of saturated hydrocarbons is obtained.

Recently a patent has been issued to Schering-Kahlbaum A.-G. (140) for the preparation of menthenes by hydrogenation of terpenes at 40–80°C. in the presence of nickel. Dipentene, one of the terpenes men-

tioned, is claimed to yield carvomenthene, i.e., menthene in which the double bond outside of the ring has been reduced.

In another patent to the same people (141) carvomenthene (1-menthene) is claimed to be converted into 2-menthane by passing its vapor over a surface catalyst, such as bleaching earth, pumice, silica gel, or "tonsil," or a metal salt such as magnesium sulfate or copper phosphate at 300–450°C.

Polymerization. Table 12, taken from the work of Staudinger and Lautenschlager (161), shows that limonene is not readily polymerized at 80°C.

On the other hand, Humphrey's patent (80) for the polymerization of dipentene in the vapor phase at temperatures ranging from 175 to 550°C. claims a yield of about 30 per cent of "dipolymer." The following example is given:

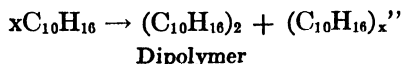
"Through an iron tube heated to about 400°, containing 8–10 mesh Fuller's earth, is passed 200 cc. of dipentene at a rate of 50 cc. per hour.

TABLE 12

Limonene

TIME	AUTOXIDATION	POLYMERIZATION IN OXYGEN	POLYMERIZATION IN CARBON DIOXIDE
<i>days</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
1	45	4	2
2	60	6	3
3	70	7	4
4	80	9	5

There were recovered 164 cc. of a product containing 62 cc. of 'dipolymer.' The reaction may be represented as



d-Limonene was found by Carter, Smith, and Read (36) to be readily polymerized to a diterpene or diterpenes ($\text{C}_{20}\text{H}_{32}$), to the extent of about 75 per cent by prolonged shaking at room temperature with syrupy phosphoric acid. α - and γ -terpinene were produced at the same time. The mechanism of this reaction will be discussed in the section on phellandrene, which exhibits the same phenomenon.

Dehydrogenation by sulfur. In Ruzicka's (128) studies of the dehydrogenation of terpenes by means of sulfur, limonene was used to determine whether the position of the side chains was altered. No rearrangement took place, for limonene was converted to *p*-cymene. The reaction may be represented as follows:

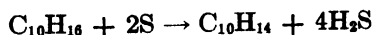


TABLE 13
Limonene and dipentene

REFERENCE NO.	HYDROCARBON	TEMPERATURE <i>degrees C.</i>	CATALYST	PRODUCTS	REMARKS
(63)	Limonene	300	—	No change	Heated in sealed tube for 4 hours
(63)	Dipentene	300	—	No change	
(65)	Carvene	Isoprene lamp	—	Isoprene	Other products not enumerated
(77)	Limonene	Isoprene lamp	—	Isoprene	Oil of <i>Pinus Serotina</i>
(99)	Limonene	450	—	Isoprene	Wood turpentine
(99)	Limonene	450	—	Isoprene	Limonene from heating of pinene
(167)	Limonene	Isoprene lamp	—	Isoprene	
(160)	Dipentene	Hot platinum coil	—	Isoprene	Vapors in high dilution with nitrogen at 2-3 mm. pressure
(196)	Limonene	180-185	Pd-Asbestos	<i>p</i> -Cymene, <i>p</i> -menthane	Atmospheric pressure
(196)	Limonene	130	Pd-Asbestos	<i>p</i> -Cymene, <i>p</i> -menthane	120 mm. pressure
(90)	<i>d</i> -Limonene	280-300	Cu	100 per cent cymene	Rate of flow 4.5 g. per hour
(90)	<i>d</i> -Limonene	200	Cu	Cymene, menthane	Rate of flow 4.5 g. per hour
(96)	Limonene	—	—	Hydrogen, gaseous hydrocarbons, hexaethylbenzene	Glow discharge
(138)	Limonene	180	Ni	<i>p</i> -Menthane	H ₂ added
(139)	Limonene	190	Cu	<i>p</i> -1-Menthene	H ₂ added and reaction allowed to go to completion
(180)	Limonene	190	Platinum black	<i>p</i> -1-Menthene, <i>p</i> -menthane	H ₂ added and reaction stopped before completion

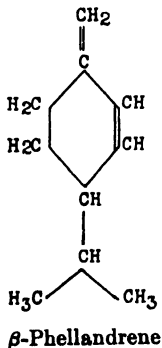
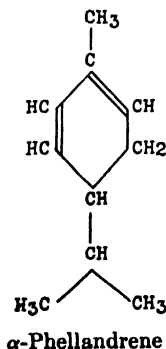
TABLE 13—Concluded

REFERENCE NO.	HYDROCARBON	TEMPERATURE	CATALYST	PRODUCTS	REMARKS
(136)	Limonene	degrees C. 350–360	Ni	<i>p</i> -Cymene, cumene, saturated hydrocarbons	H ₂ added
(80)	Limonene	400	Fuller's earth	Dimer, polymer	50 cc. per hour through iron tube
(128)	Limonene	ca. 180	S	<i>p</i> -Cymene	Terpene re-fluxed with sulfur
(172)	Limonene	—	Ni	Cymene and menthane	
	Limonene	—	Cu	Cymene and menthane	
(141)	Carvomenthene (Δ^1 -menthene)	300–450	Bleaching earth, pumice, silica gel, tonsil, MgSO ₄ , CuSO ₄ , etc.	Δ^1 -Menthene	
(36)	<i>d</i> -Limonene	Room temperature	H ₃ PO ₄	A dipentene, α - and γ -terpinene	

The details of the procedure are given in the section on sesquiterpenes, since the method has been used as a tool in determining the structure of some of the sesquiterpenes.

Table 13 summarizes the results obtained from the thermal treatment of limonene and dipentene with and without catalysts.

2. Phellandrene



Although the phellandrenes have been known for some time, it was not until the work of Wallach that their structures were clearly established. They are so unstable that they decompose to some extent when distilled at ordinary pressure (155), and readily resinify and lose rotatory power on exposure to air so that it is difficult to obtain them in pure condition. This marked instability is due, in part at least, to conjugated double bonds.

Polymerization. Pesci (116) has reported that these hydrocarbons polymerize by repeated distillation and if heated for twenty hours in a sealed tube are converted to a glassy mass, $(C_{10}H_{16})_x$.

Semmler and Jonas (152 and 153) found that both α - and β -phellandrene polymerize when heated to about 300°C. The product in the case of

TABLE 14
Formation of diterpenes by action of H_3PO_4 on monoterpenes

SOURCE	APPROXIMATE YIELD OF CRUDE DITER- PENE	BOILING POINT	$[\alpha]_D^{20}$
	<i>per cent</i>	<i>degrees C.</i>	
<i>l</i> - α -Phellandrene.....	40	182-184 at 16 mm.	+14.96
<i>E. dives</i> oil.....	50	193-195 at 24 mm.	+13.20
<i>E. phellandra</i> oil.....	40	194-196 at 24 mm.	+3.28
<i>M. acuminata</i> oil.....	45	191-193 at 22 mm.	+1.00
<i>d</i> -Limonene.....	75	192-194 at 23 mm.	+0.16
<i>d</i> -Pinene.....	75	179-181 at 13 mm.	-0.10
<i>l</i> -Pinene.....	75	197-200 at 29 mm.	+0.07

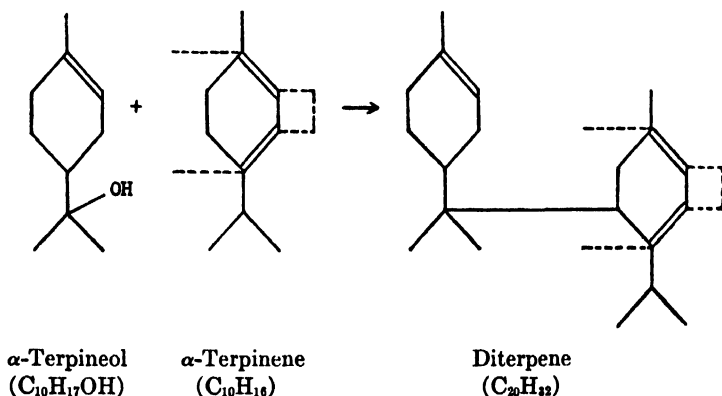
the α -compound is a diterpene, b.p. 175-185°C., $n_D - 6^\circ$. From the β -compound the product is also a diterpene, b.p. 175-185°C., but it has a rotation of +9.5°.

Carter, Smith, and Read (36) found that after prolonged shaking with syrupy phosphoric acid *l*- α -phellandrene yielded 40 per cent of a diterpene ($C_{20}H_{32}$) along with α - and γ -terpinene. Parallel experiments with other terpenes led to similar results; the chief products in all instances appearing to be α -terpinene and a diterpene, or a mixture of diterpenes, both of which strongly resisted the further action of phosphoric acid at ordinary temperatures.

The results obtained are shown in table 14.

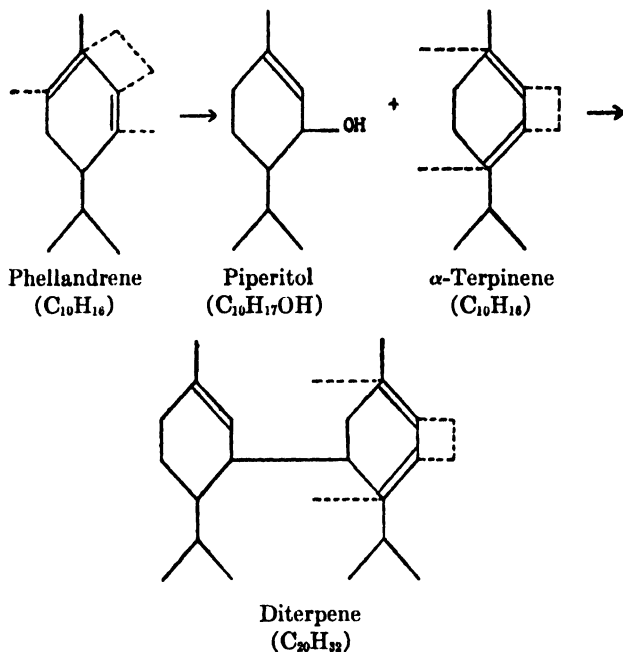
The following points are worthy of interest: absence from the products of limonene (except in the case where that substance was used), dipentene, or terpinolene; practical identity of physical constants of the diterpenes,

except for optical activity; failure to obtain crystalline derivatives of any diterpene; stability of the diterpenes to distillation at ordinary pressure, in contrast to colophene ($C_{20}H_{32}$) which breaks down; and the corresponding formation of a similar diterpene from cineole, the reaction mixture of which yielded terpin hydrate. These facts "point to the formation in all of these instances of an optically active intermediate product, such as the symmetrical substance, terpin. By dehydration and isomerization this substance could give rise to α -terpineol, α -terpinene, etc.; moreover it appears likely that the diterpene is formed as the intermediate result of condensation between the hydroxyl group of a molecule of the first type and an activated hydrogen atom of a terpene molecule, rather than by polymerization of two terpene molecules. In the appended possible scheme, it is seen that the hydrogen atoms attached to carbon atoms 5, 6, 7, or 8 of the α -terpinene molecule may be regarded as activated owing to their relationship to the conjugated system formed by the remaining carbon atoms of the ring:



"Even for the specific scheme here postulated, condensation might conceivably occur either at position 5, 6, 7, or 8 in the α -terpinene molecule. Altogether, therefore, it would seem that all specimens of diterpenes produced in such ways are likely to consist of complex mixtures of isomerides, which may possibly afford some explanation of their reluctance to crystallize or yield crystalline derivatives.

"The optical activity of the diterpene from *l*- α -phellandrene calls for a mechanism which does not involve intermediate conversion to an optically inactive substance, and the following scheme may be brought forward in illustration of the various possibilities:"



Catalytic hydrogenation. Like limonene, β -phellandrene has been found (140) to yield a menthene when hydrogenated at 40–80°C. in the presence of a nickel catalyst.

TABLE 15
Phellandrene

REFER- ENCE NO.	HYDROCARBON	TEMPERATURE <i>degrees C.</i>	PRODUCTS	REMARKS
(116)	Phellandrene	Not given	$(C_{10}H_{16})_x$	Heated in sealed tube
(152) } (153) }	Phellandrene α - or β -	300	Diterpene	
(152) } (153) }	α - or β -Phellandrene + isoprene	300	Sesquiterpene	
(90)	Phellandrene	300	<i>p</i> -Cymene, menthane	Cu catalyst
(140)	β -Phellandrene	40–80	<i>p</i> -2-Menthene	Ni catalyst
(36)	<i>l</i> - α -Phellandrene	Room temperature	A diterpene, α - and γ -terpinene	H_3PO_4 catalyst
(172)	Phellandrene	—	<i>p</i> -Cymene, menthane	Ni or Cu catalysts

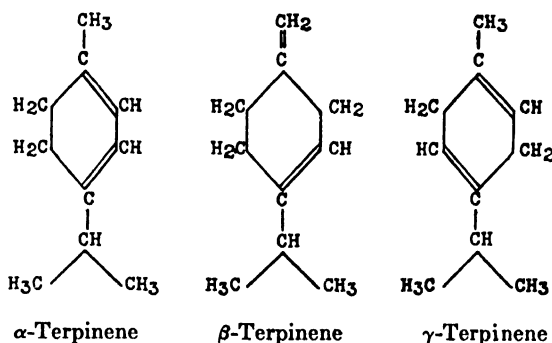
When either α - or β -phellandrene is heated with isoprene to about 300°C., a sesquiterpene is formed. In the case of the α -compound the product boils at 129–132°C. under 15 mm. pressure and has a rotation of -15° , while the β -compound yields a sesquiterpene boiling at 137–140°C. under 15 mm. pressure and having a rotation of $+4^\circ$.

Komatsu and Kurata (90) have shown that phellandrene is converted to cymene and menthane when passed over finely divided copper at 300°C.

Treibs and Schmidt (172) obtained the same result by using nickel and copper catalysts.

A summary of the results obtained from treating phellandrene is given in table 15.

3. Terpinene



Non-catalytic decomposition. According to Staudinger and Klever (160) terpinene gives little or no isoprene when refluxed in an isoprene lamp.

Catalytic decomposition. Zelinsky and Lewina (200) have extended the former's studies of non-reversible catalysis to include α -terpinene. This

TABLE 16

Terpinene

TIME	AUTOXIDATION	POLYMERIZATION IN OXYGEN	POLYMERIZATION IN CARBON DIOXIDE
days	per cent	per cent	per cent
1	57	6	3
2	73	8	5
3	78	9	7
4	83	12	8

compound, like other terpenes, yields *p*-cymene and *p*-menthane when passed slowly in a stream of carbon dioxide over palladinized asbestos at 190°C.

Hydrogenation. Like sylvestrene, terpinene has been found by Sabatier

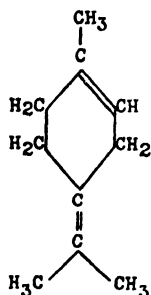
and Senderens (138) to yield *p*-menthane on hydrogenation with a nickel catalyst at 180°C.

Incomplete hydrogenation of β -terpinene (140) at 40–80°C. in the presence of nickel yields *p*-3-menthene.

Polymerization. Terpinene is very much like limonene in its behavior on being heated at 80°C. for four days. Staudinger and Lautenschlager's (161) data on the per cent polymerized and oxidized at given time intervals are presented in table 16.

Dehydrogenation with sulfur. Terpinene, like limonene, was used by Ruzicka (128) to test his dehydrogenation method using sulfur. In this case he obtained an even better yield of *p*-cymene than from limonene.

4. Terpinolene



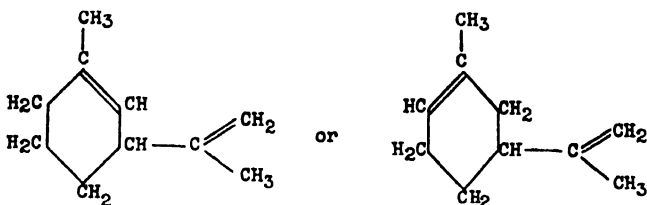
Terpinolene is a comparatively unstable terpene which, as Wallach (184) observed, is easily converted to its isomer, terpinene, by the action of halogen acids or acetic acid solutions in the cold. Wallach does not indicate, however, which isomer is formed.

Non-catalytic decomposition. Staudinger and Klever (160) found that this hydrocarbon yields only a little isoprene when its vapors are passed over a hot platinum filament.

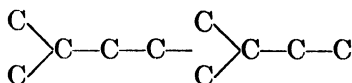
Catalytic decomposition. Mailhe (100) has reported a rather detailed study of the pyrolysis of terpinolene using reduced copper as a catalyst. At 500–550°C. the following products were obtained: (1) gaseous olefinic and paraffinic hydrocarbons and hydrogen, (2) benzene, (3) toluene, (4) methylcyclohexane, (5) *m*-xylene, and (6) *m*-cymene.

The absence of isoprene is a little conspicuous, but Mailhe pointed out that any isoprene formed might well have been hydrogenated at such a high temperature in the presence of the large amount of hydrogen produced in the process.

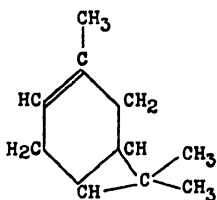
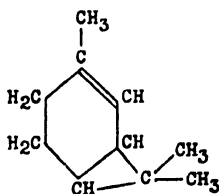
When passed over palladinized asbestos at 160–170°C., terpinolene (200) yielded *p*-cymene and *p*-menthane.

5. *Sylvestrene**(dl-Sylvestrene = carvestrene)*

Until recently sylvestrene was considered a natural product and, as such, was an enigma, for it did not fit in with Ingold's (83) suggestion that terpenes were built up by the union of two isoprene molecules forming the geranial chain



with subsequent condensation to the *p*-cymene type of ring. The absence of sylvestrene in naturally occurring oils was established by Rao and Simonsen (121), who showed that it resulted from the action of hydrochloric acid on *d*-3-carene or *d*-4-carene.

*d*-3-Carene*d*-4-Carene

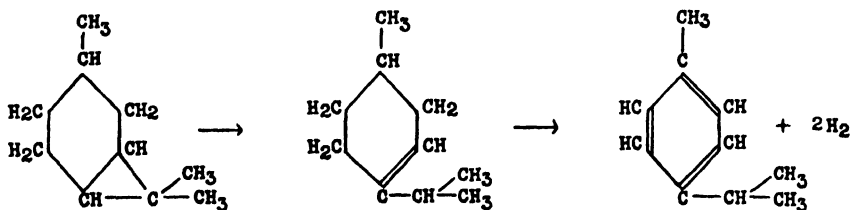
Pyrolysis. The fact that sylvestrene and its *dl*-form, carvestrene, were such a puzzle may have been a determining factor in the study of their pyrolysis, in spite of the fact that their relation to *m*-cymene was made known by Baeyer and Villiger (12) in 1898. Whatever the cause may be, the fact remains that the only reference found concerning sylvestrene's reaction toward heat is a brief one made by Wallach (187), in which he states that sylvestrene is a very stable hydrocarbon and shows no tendency to isomerize when heated in a sealed tube at 250°C.

Catalytic hydrogenation. Sabatier and Senderens (138) have found that sylvestrene yields *p*-menthane or hydrocymene when passed over nickel at 180°C. in the presence of hydrogen. In order to obtain these products a rearrangement must have taken place, for sylvestrene is a meta compound.

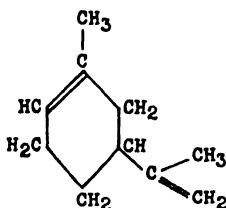
On the other hand, the patent to Schering-Kahlbaum A.-G. (140), referred to previously, indicates that *m*-1-menthene is the product of partial hydrogenation of sylvestrene at 40–80°C. in the presence of nickel.

Since carene is the precursor of sylvestrene, it is of interest to note Zelinsky's (199) work on carane, $C_{10}H_{18}$. When carane is passed over platinized charcoal at 160°C. in a stream of hydrogen, *p*-menthane is formed. Zelinsky compares his results with those of Semmler, who had found that carane was not reduced by hydrogen and platinum black at ordinary temperatures.

Irreversible catalysis. In the study of dehydrogenation by means of platinized charcoal at 300°C. in the presence of carbon dioxide, Zelinsky (199) found that carane underwent the following changes:



6. Diprene

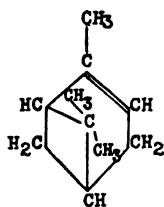
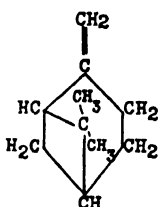
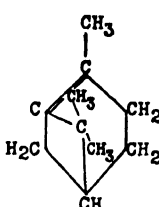
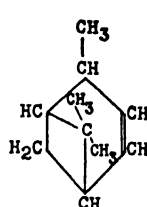


Diprene, a synthetic terpene, has been isolated from the polymerization products of isoprene. Earlier in this paper (182) it has been pointed out that the 2,6-dimethyloctatriene of Harries (61), the diprene of Aschan (6), and the β -myrcene of Ostromisslensky (114) are identical. Furthermore, as the above formula indicates, they are shown to be cyclic compounds rather than acyclic as Harries and Ostromisslensky had thought.

Polymerization. Ostromisslensky (114) polymerized diprene (β -myrcene) by shaking it with sodium and barium peroxide at 60–70°C. for five days, and found that it gave a quantitative yield of the same "normal isoprene caoutchouc" as that obtained from the polymerization of isoprene at "high temperatures." Under these conditions natural myrcene remained unchanged, while isoprene yielded an "isomeric abnormal caoutchouc."

C. DICYCLIC TERPENES

1. Pinene

 α -Pinene β -Pinene γ -Pinene δ -Pinene

Pinene occupies a rather enviable position in the field of terpene pyrolysis for, in spite of the fact that it is a bicyclic terpene, it has been the

TABLE 17
Turpentine components

TURPENTINE	COMPONENTS							
	α -Pinene	β -Pinene	Limone + dipentene	Carene	Other terpenes	Sesquiter- penes	Heptane	Residue
	per cent	per cent	per cent	per cent	per cent	per cent	per cent	per cent
Bordeaux (<i>Pinus Maritima</i>).....	62.6	26.8	—	—	—	—	—	10.6
American (longleaf and spruce pine)...	71	29	—	—	—	—	—	—
Longleaf pine (Dupont 80).....	64.3	31.8	—	—	—	—	—	—
Cuban.....	75.6	21.2	—	—	—	—	—	—
Russian (Dupont).....	72	28	—	—	—	—	—	—
Russian (Krestinsky (56)).....	42.5	—	—	32.5	4	3	—	18
Indian (<i>Pinus Longifolia</i>).....	24.8	9.7	—	37.6	1.7	20.3	—	5.9
Chinese.....	85	—	—	—	—	11	—	—
Alpine (<i>Pinus Halepensis</i>).....	95	—	—	—	—	3.8	—	1.14
Italian (<i>Pinus Pinea</i>).....	—	—	90	—	—	10	—	—
French (<i>Pinus Serotina</i>).....	—	—	90	—	—	10	—	—
Western U. S. (<i>Pinus Sabiniana</i>).....	—	—	—	—	—	—	90	—

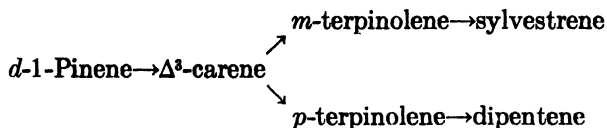
most extensively studied. The term pinene, which should be replaced by the plural "pinenes," is used rather indiscriminately throughout the literature, so that there is no way of determining which of the four isomers some investigators used. In the few cases where the particular isomer was designated, that information has been carried into this paper. In the majority of cases where the term "pinene" occurs, the assumption may be made that the material was a mixture of α - and β -pinenes obtained by fractionation of some naturally occurring product, for the other two

isomers, γ - and δ -, have been prepared from natural oils but do not occur in them.

The most obvious reasons for the extensive study of pinenes are (1) the value of the isoprene obtained and (2) the abundance of the pinenes in turpentine and other relatively inexpensive naturally occurring oils. Quoting from Dupont (41), "The majority of the oils of turpentine have pinenes as their principal constituents; among these α -pinene always dominates and is sometimes the exclusive constituent. These terpenes always appear to be accompanied by a certain proportion of sesquiterpenes. However, in some turpentines other terpene constituents appear and even dominate, for example, limonene, carene and others and even hydrocarbons of nonterpeneic nature as heptane."

Since pinene is the chief constituent of most turpentines, the pyrolysis of turpentine has been included in this section. Wherever given by the investigator, the source of the turpentine used is stated. Table 17 compiled from Dupont's (41) survey and other recent publications gives what is known of the composition of the turpentines included.

With respect to carene and the terpenes other than the pinenes found in Russian turpentine (2), it has been claimed by Lyubarskii (98) that their presence is due to the fact that *d*-1-pinene can isomerize in the following manner:



Early work. The earliest reference to the pyrolysis of turpentine seems to be in the work of Gay-Lussac and Lariviere in 1841 (55), who found that turpentine yielded some oils that were more volatile than turpentine and others less volatile.

Some twenty years later Berthelot (14) found that French turpentine could be refluxed for sixty hours in an atmosphere of carbon dioxide with little change in rotatory power or other properties. However, when French, English, or Swiss turpentine was heated in closed tubes at 250°C. for ten hours, polymerization took place, accompanied by change in rotation but without gas formation. From the polymeric substances he isolated the two chief constituents and designated them as iso- and meta-turpentine. English turpentine heated for two hours at 300°C. also yielded "isoturpentine," b.p. 176–178°C. This substance differed from "metaturpentine" in that it added two molecules of hydrogen chloride for every three molecules of $C_{10}H_{16}$, while "metaturpentine" added an equimolar quantity of hydrogen chloride based on the molecular weight of $C_{10}H_{16}$.

In 1860 Schiel (144) reported that the dry distillation of "colophonium" (turpentine) yielded "colophonon," an oxidation product, and "tereben" a $C_{10}H_{16}$ hydrocarbon.

Hlasiwetz and Hinterberger (79) passed turpentine through a red-hot iron tube filled with porcelain sticks. They obtained a gas, carbon, and a dark brown oily liquid condensation product. They isolated a hydrocarbon C_8H_8 , b.p. 60–70°C., and an isomer of "terpintinol."

A year after this preliminary note by Hlasiwetz, Berthelot (16) observed that turpentine, passed through a porcelain tube at a moderate red heat, underwent radical change. In the fraction boiling below 250°C. the following products were identified: benzene, in small quantity; toluene, principal product; xylene, notable quantity but less abundant than toluene; cumolene, still less abundant; cymene, a very small amount; and naphthalene, notable quantity. No mention was made of any products more volatile than benzene, although such were probably formed.

Schultz (148) dropped turpentine into an iron tube which was maintained at dull red heat. There was a large amount of gas liberated, which was assumed to be a mixture of hydrogen and hydrocarbons and was allowed to escape. From the fraction of the liquid products boiling below 200°C., he isolated benzene, toluene, *m*-xylene, naphthalene, anthracene, methylanthracene, and phenanthrene, but again no substances of lower boiling point than benzene were identified.

In Tilden's (171) study of the pyrolysis of American turpentine, the commercial oil was fractionated and only that portion boiling between 156 and 160°C. was used.³ This fraction was boiled in a copper flask and the vapors passed through an iron tube heated to the first visible redness. From 4 liters of turpentine there were collected 1275 cc. of liquid boiling below 140°C., 850 cc. boiling between 140 and 200°C., and 650 cc. of material boiling above 200°C. The remainder was accounted for in the gas produced, slight loss by evaporation, and deposition of sooty carbon.

The fraction up to 30°C. was reported to contain some acetylene by reason of the formation of a small quantity of a greenish-yellow precipitate on the addition of ammoniacal cuprous chloride.

From the fractions up to 150°C. benzene, toluene, *m*-xylene, and a "hydrocarbon which is probably identical with the heptene⁴ of rosin spirit" were obtained, but "the chief volatile ingredient here is a pentine,

³ Since Vavon (180) has concluded that α - and β -pinene are the only constituents of that fraction of turpentine boiling between 135 and 165°C., it is reasonable to consider that Tilden's investigation was made on a mixture of these two isomers.

⁴ This "heptene" (C_7H_{12}) is not an acetylene hydrocarbon but a homolog of isoprene, i.e., a diolefin.

b.p. 33–35°C., C_6H_8 (isoprene), and it would seem, therefore, that the original terpene is more readily depolymerized than is the optically inactive isomeride 'terpilene' (dipentene) which also results from the action of heat upon it." (See Wallach, Mahood, and others on rearrangement of pinene to dipentene.)

With regard to the yield of isoprene obtained, Mokiewski (107) has pointed out that Tilden's isoprene fraction was probably 50 per cent trimethylethylene, for trimethylethylene is formed in the pyrolysis of turpentine and cannot be separated from isoprene by distillation.

In the fraction boiling at 150–180°C. "terpilene (dipentene) is present, but on treating the portion which came over between 170 and 180° with small quantities of sulfuric acid and then steam-distilling, it yielded more than half its volume of cymene, the presence of which effectually prevented the isolation of the dihydrochloride of terpilene (dipentene) in a crystalline state."

When the vapors of the above fraction of turpentine were passed through the iron tube heated to bright redness, a large quantity of gas was evolved, with some liquid of which the most volatile constituent was benzene. It was only at the lower temperatures that an appreciable quantity of low-boiling liquid products was obtained. As a consequence of these results, Tilden pointed out that the difference in the results obtained by Schultz (148) and Hlasiwetz (79) was probably due to a difference in temperature, the temperature of the tube in the Schultz experiments being much higher than in those of Hlasiwetz.

Non-catalytic decomposition. In 1904, Mokiewski (108) pyrolyzed 40 kg. of turpentine oil (b.p. 155–156°C.) by passing it through a glass tube at dull red heat. He obtained gases containing ethylene and propylene, 300 g. of material (b.p. 20–30°C.) containing divinyl and butylene, 2500 g. of material (b.p. 30–40°C.) consisting for the most part of isoprene and trimethylethylene, 700 g. of material (b.p. 70–80°C.) consisting of 10 per cent of benzene and also containing olefins and diolefins, 400 g. of material (b.p. 95–110°C.) consisting of 60 per cent of toluene, and also olefins and diolefins, and finally 400 g. of material (b.p. 95–100°C.) consisting of more than 75 per cent of xylene.

Except for the work of Mokiewski there seems to have been little interest in the pyrolysis of pinene or turpentine from about 1884 to 1909. In 1909 this subject came to the fore because of the developments in research on synthetic rubber and the consequent need of a cheap source of isoprene.

Harries and Gottl b (65) obtained a 1 per cent yield of isoprene from commercial *d*- and *l*-pinene by means of the isoprene lamp. However, they attributed the formation of isoprene to limonene present as impurity in pinene. In addition to the isoprene, gaseous compounds were liberated, while thick saturated oils of high boiling point remained in the flask.

Contrary to the assumption of Harries and Gottl b, Herty and Graham (77) have shown that isoprene is formed from pinene. They separated turpentine into fractions boiling at 155–156 C., 169–175 C., and above 175 C. The first fraction should be primarily pinene, and the second and third should include all of the dipentene or limonene. They used a modified isoprene lamp and obtained an 8 per cent yield of isoprene from the pinene fraction, a 0.5 per cent yield from the middle fraction, and no isoprene from the highest boiling fraction. Turpentine without fraction-

TABLE 18
Pyrolysis of turpentine

MATERIAL USED	TUBE AND CONTENTS	TEMPERATURE	ISOPRENE
		degrees C.	per cent
Fraction of wood turpentine boiling 150–180�	Pyrex tube (empty)	450	0.0
		500	0.75
		550	3.0
		600	4.5
		650	2.7
		700	2.5
Fraction of wood turpentine boiling 150–180�	Pyrex filled with porcelain chips	350	0.0
		400	0.5
		450	2.5
		500	4.4
		550	4.0
		600	Av. = 4.5
Wood turpentine (not fractionated)	Pyrex tube with CuO and CuCl ₂	450	1.5
		500	2.0
		550	2.5
		600	2.5
		650	Tube plugged by carbon deposition
Gum turpentine (not fractionated)	Iron tube (empty)	450	Av. = 4.98
		500	0.5 ?

ation yielded 5.5 per cent of isoprene, but no information was given concerning the nature of the other products obtained.

Schorger and Sayre (146) are in agreement with Herty and Graham's opinion that the formation of isoprene from turpentine is not due to the dipentene or limonene present. They have shown that under the same conditions turpentine and α - and β -pinene yield about the same amount of isoprene, approximately 10 per cent.

The thermal decomposition of turpentine has also been studied by Mahood (99), who found that when the vapors were passed through an empty Pyrex tube the maximum yield of isoprene was obtained at 600 C., while

when the same tube was filled with porcelain 500°C. appeared to be the optimum temperature. When this tube was filled with a mixture of copper oxide and cupric chloride, prepared according to the patent issued to Gross (58), there was no increase in yield, although Gross claimed a 40 per cent yield of isoprene from turpentine. With an iron tube and no contact material the most suitable temperature for the production of isoprene appeared to be 450°C.

Wood turpentine, which contains a considerable amount of limonene, might be expected to give a larger yield of isoprene than gum turpentine according to Harries, but Mahood's results do not confirm this. Table 18 compiled from Mahood's data serves to illustrate this.

"Complete analyses of the various fractions were not made, but qualitative tests showed considerable quantities of terpenes in the higher boiling fractions obtained in cracking at lower temperatures, while hydrocarbons of the benzene series and olefinic hydrocarbons are the chief constituents of all fractions formed at cracking temperatures above 400°."

Toluene was found to be a chief constituent of the fraction boiling between 100–125°C. Cymene was identified in the fraction boiling between 165 and 180°C. and *m*-xylene in the fraction boiling at 150 to 165°C. "The gas formed had an odor somewhat similar to coal gas and burned with a luminous flame. Of this material 10 to 22.5 per cent by volume dissolved in fuming sulfuric acid, showing that olefins were present to that extent."

Non-catalytic decomposition in the presence of diluents or under reduced pressure. Staudinger and Klever (160) have found that turpentine yields a very small amount of isoprene when the vapors in high dilution with nitrogen or under 2–3 mm. pressure are passed over a hot platinum coil. However, they point out the fact that contrary to the results obtained by earlier investigators (107), the isoprene fraction contains very little trimethylethylene. On the other hand, Prodrom (120) has reported that the decomposition of pinene in vacuo at "high" temperatures gives the following components: crude distillate, 42 per cent (crude isoprene, 25 per cent); residue, 44 per cent; and losses due to gas, 14 per cent.

A patent to Silberrad (154) for the production of isoprene by heating turpentine under reduced pressure gives the following results: "Eight liters of turpentine were passed through a metallic tube heated to 550°, and the pressure was reduced to 5–16 mm. The products obtained were 24 cc. of a liquid, b.p. 5–16°, 723 cc. crude isoprene, 537 cc. benzene, toluene, xylene, etc., and 6686 cc. unchanged turpentine but no sesquiterpene or resin. Calculating the yield of isoprene on the basis of turpentine converted, the yield of crude isoprene is 55 per cent and pure isoprene

35 per cent. At the same temperature but about 200 mm. pressure the yield of crude isoprene is only 33 per cent and that of sesquiterpene and resin 9.2 per cent."

In 1909 Woltereck (193) obtained a patent covering the production of isoprene by passing turpentine mixed with nitrogen through an iron tube filled with inert material, such as wire gauze or perforated disks, the purpose of the inert material being to augment the contact surface. He stated that the yield of isoprene was proportional to the dilution and claimed a better yield than Tilden. However this means little, for Tilden's yield, based on his own figures, was less than 5 per cent and according to Mokiewski's statement, was less than 2.5 per cent.

Heinemann (71) patented the use of steam as a diluent for turpentine vapors. The mixed vapors were passed through a tube of suitable metal or refractory material at a temperature of about 750°C. The temperature range specified is from 650–950°C., as temperatures above 950°C. are not suitable because of the decomposition of the water. At 750°C. Heinemann claims a 40 to 50 per cent conversion of the turpentine into hydrocarbons boiling below 100°C., 60 per cent of which is isoprene.

Some years after these patents were issued, Ostromisslensky (113) stated that the gases and liquid hydrocarbons boiling between 60 and 150°C., obtained from the pyrolysis of turpentine, might be used as diluents for the pyrolysis of additional quantities of turpentine.

Catalytic decomposition. Undoubtedly some of the early work on the pyrolysis of turpentine might be classed as catalytic. For example, it will be shown in the following paragraphs that iron has a definite catalytic effect in this reaction, and Hlasiwetz, Schultz, and Tilden used iron tubes for their experiments. Since this is the case, the work of Sabatier, Mailhe, and Gaudion (137) may be considered as a continuation of some of the early work, for they have included iron in their study of the effect of different metals at different temperatures.

Using finely divided copper maintained at 500°C., the products from the pyrolysis of pinene were (1) a large quantity of gas which contained hydrogen and ethylenic hydrocarbons, (2) an 8 per cent yield of a greenish liquid boiling below 120°C., (3) a 5.9 per cent yield of a liquid boiling between 120 and 150°C., (4) a 76.1 per cent yield of liquid boiling between 150 and 185°C., and (5) a 10 per cent yield of products boiling above 185°C.

With copper at 600–630°C. more gas was formed, the low-boiling fraction was amber colored, and a tarry residue was deposited on the catalyst. A liquid fraction amounting to 13.3 per cent, which boiled below 95°C., contained a small amount of benzene and toluene with isoprene, 1,3-

pentadiene, amylene, and hexene. The next fraction, boiling range 95–150°C., of which there was 27 per cent, was made up of 63 per cent ethylenic compounds and the remainder aromatics. The third fraction, comprising 31.4 per cent and boiling at 150–185°C., contained cumene, cymene, methylbenzene, and terpenes isomeric with pinene. The last fraction, of which there was 9 per cent, was made up of condensed terpenes, olefins, and diolefins and boiled above 185°C. The total amount of aromatics formed at 600–630°C. was about 31 per cent, much more than the amount produced at the lower temperature.

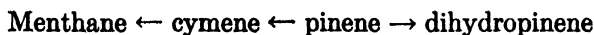
Nickel at 600°C. caused a very energetic decomposition of pinene, and the reaction differed from that with copper in that there was an abundant deposition of carbonaceous material. The gas liberated was rich in hydrogen and little liquid condensed. The activity of the metal soon diminished, as carbonaceous material deposited on it, and with this diminution the gas became less abundant, and the reaction products resembled those formed in the presence of copper. This may be due to carbon acting as a catalyst in both cases.

Cobalt at 600°C. gave results intermediate between those of copper and nickel. Iron acted more like nickel, causing intense charring.

Heinemann (72) was granted patents for the production of isoprene by passing turpentine through copper or silver tubes or over finely divided copper or silver at temperatures of 480° and 450°C., respectively. He claimed good results with a copper tube of 6 mm. diameter and 4 meters in length closely wound into a coil. With a rate of flow of vapors of 2000 cc. per hour, a yield of 25 per cent of isoprene is claimed. Heinemann warns that the higher the temperature the more polymerization there is of isoprene to dipentene.

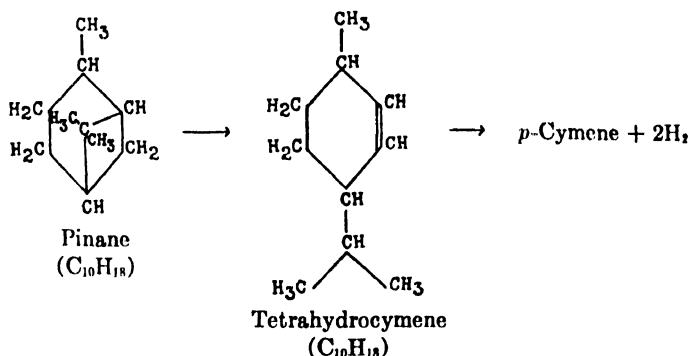
A few years after this patent was issued, Stephan (166) obtained a patent for the production of isoprene by passing nopinene (β -pinene) over iron or other metal so that the nopinene was heated above 600°C.

In the course of his investigations of irreversible catalysis, Zelinsky (197) found that either *d*- or *l*-pinene yields a mixture of cymene and dihydropinene when the vapors are mixed with carbon dioxide and passed over palladinized asbestos at 190–200°C. The mixture of cymene and dihydropinene was passed through the same tube containing palladinized asbestos at 200°C. and again at 150°C. The final product was a mixture of menthane and dihydropinene, and the reaction was outlined as follows:



The dihydropinene (pinane) resulting from the above reaction was dehydrogenated by Zelinsky and Lewina (199) to *p*-cymene. The equation

for the reaction in the presence of carbon dioxide and platinized charcoal at 300°C. is as follows:



Zelinsky and Lewina (200) later extended their study of irreversible catalysis to nopinene (β -pinene). When this hydrocarbon is passed over palladinized asbestos at 190°C. at the rate of six to eight drops per minute, a mixture of *p*-cymene and dihydropinene is obtained. Like α -pinene, then, the beta compound, in contact with palladinized asbestos, undergoes simultaneous hydrogenation and dehydrogenation. The suggestion is offered that β -pinene is first converted to the α -form.

Treibs and Schmidt (172) found that nickel and copper catalysts exhibited a somewhat similar behavior, transforming β -pinene into cymene and pinane.

Freund (48) treated French turpentine, containing *l*-pinene as its chief constituent, with anhydrous aluminum chloride under varying conditions, until solid or semisolid polymers were obtained. These polymers were then pyrolyzed at temperatures up to about 360°C. It was found that the resulting hydrocarbon fractions closely resembled those obtained from Java petroleum, particularly with respect to their optical rotations. Freund therefore concluded that terpenes were present among the mother substances of petroleum.

Previously Steinkopf and Freund (165) allowed aluminum chloride to react with turpentine oil, first at ice bath temperatures and then for various periods at room temperature, and obtained liquid and solid products along with considerable unchanged turpentine. The solid was a brittle substance (m.p. 77–78°C.) having the formula $(C_{10}H_{16})_x$.

Similar treatment of pure *l*-pinene gave the same result.

When the aluminum chloride was added with vigorous stirring a "tough mass" resulted, and if this was then heated, liquid and gaseous products were formed. From 200 g. of turpentine there was obtained 3.5 l. of

gas, 126 g. of liquid, and about 100 g. of residue, including the aluminum chloride.

The gas consisted chiefly of paraffin hydrocarbons, with some cycloparaffins, and traces of unsaturates.

The following substances from the liquid product were identified by means of physical constants: pentane, isopentane, trimethylethylmethane (?), octanaphthene, various polynaphthenes not absolutely identified, fractions containing mixtures of C_nH_{2n-2} and C_nH_{2n-4} hydrocarbons, and possibly dihydropinene. Decanaphthene and benzene were identified by nitration. There was also obtained a high-boiling fraction resembling natural lubricating oil.

Routala (124) treated Finnish turpentine oil with condensation agents such as zinc chloride, alumina and chlorine, aluminum bromide, and aluminum chloride. The latter was the most effective. A turpentine fraction (b.p. 160–167°C.) yielded a mixture of paraffin, olefin, polyolefin, and naphthene hydrocarbons, similar in composition to ordinary petroleum. Ethyl and methyl chlorides were also produced.

Crude or partially purified turpentine oil gave, on treatment with aluminum chloride, principally semisolid pitchy substances.

Electrical decomposition. Berthelot (17) observed that no gas was liberated by the action of the electrical discharge on pinene, but that a slight rise in temperature resulted. The liquid was not discolored, and most of the pinene was recovered unchanged. There was isolated, however, a small amount of a diterpene formed by the polymerization of pinene. This polymerization, though slow, was especially clean cut in an atmosphere of nitrogen or hydrogen.

Urbain (176) reported that ethylene, acetylene, isoprene, and other substances were produced by the action of the electric arc on pinene.

The decomposition of pinene in a glow discharge has been carried out by Linder and Davis (96). The gases produced are hydrogen, acetylenes, olefins, and paraffins, but it is worthy of note that these gases are produced at a very much slower rate than in the case of limonene and dipentene. The solid product identified was *p*-diphenylbenzene.

Catalytic hydrogenation and dehydrogenation. Sabatier and Gaudion (136) have done some interesting work on the hydrogenation of pinene, using various metals as catalysts. They point out that it is well-known that the hydrogenation of benzene hydrocarbons, cyclohexenes, and terpenes, under the action of nickel at temperatures in the neighborhood of 180°C., yields the corresponding cyclic hydrocarbons or cycloalkanes. In particular, pinene (138) forms the dihydride without any secondary reaction, but the phenomenon changes its aspect when the temperature is raised.

If the vapors of pinene, carried along by hydrogen, are directed onto a column of nickel maintained at 350–360°C., a liquid is obtained which distills at 160–175°C. and is composed of hydrocarbons—cumene, probably menthane (rather than pinane) and, above all, cymene—resulting from simultaneous hydrogenation and dehydrogenation. The presence of hydrogen is indispensable for the reaction, for if the current of hydrogen is stopped, pinene gives only a mixture of terpenes, the principal constituent of which is dipentene. The main reaction in this case, then, is a simple isomerization by heat.

Turpentine has also been treated in the above manner and, as would be expected, was converted into a complex mixture which contained little benzene but an abundance of cyclic and diethylenic hydrocarbons.

Zelinsky and Lewina (199) found that when *l*-pinene was mixed with hydrogen and the vapors passed over palladinized asbestos at 195–200°C., a dihydro product was obtained which was identical with dihydropinene.

TABLE 19

Pinene

TIME	AUTOXIDATION	POLYMERIZATION IN OXYGEN	POLYMERIZATION IN CARBON DIOXIDE
<i>days</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
1	44	2	1
2	55	3	2
3	70	4	3
4	86	5	4

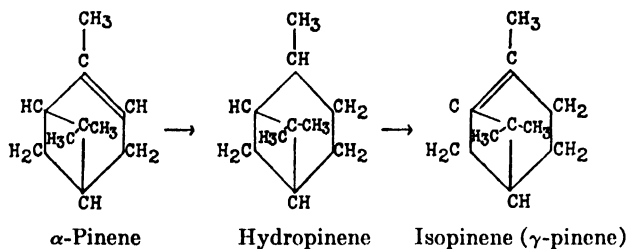
However, when *d*- α -pinene was used and the temperature changed to 157–158°C., the dihydro product boiled at 169–169.5°C. instead of 166.5–167.5°, the boiling point of dihydropinene. This fact, as indicated by Zelinsky, shows that catalytic reduction of pinene varies according to the temperature.

Rearrangement and polymerization. (1) *Elevated temperatures.* As has been stated previously, Wallach (184) discovered the conversion of pinene to limonene by heat, and Mahood used this procedure to prepare dipentene. Recently Conant and Carlson (32), from their study of the rate of isomerization, have indicated that fifty hours heating at 200°C. is necessary for the complete conversion of pinene to dipentene.

As Kassel (86) points out, this reaction is of particular interest, for it is the only known example of a presumably unimolecular rearrangement, while all other first-order gas reactions are decompositions. Smith (156) had determined the order of the reaction but considered it a racemization rather than a rearrangement.

(2) *Elevated temperatures in the presence of oxygen.* The relative rate of autoxidation and polymerization of pinene at 80°C. was studied by Staudinger and Lautenschlager (161), and the relationships shown in table 19 were determined.

(3) *Catalyzed by hydrogen and palladium black.* In some earlier work Zelinsky (195) found that α -pinene obtained from French turpentine oil (levo) was isomerized at room temperature by the action of palladium black covered with anhydrous ether and saturated with hydrogen. The isopinene so formed was supposed to be produced from a hypothetical intermediate, hydropinene, as follows:



It is of interest to note that the structure which Zelinsky gives for isopinene is contrary to Bredt's rule (82).

It was observed by Richter and Wolff (122) that an almost quantitative conversion of β -pinene into α -pinene resulted when the former was shaken with palladium and hydrogen at room temperature. If the reaction was allowed to continue indefinitely, hydrogenation to pinane resulted.

(4) *Catalyzed by salts and weak acids.* Berthelot (15) in 1853 observed that boron trifluoride readily transformed pinene into a polymer (boiling at 300°C. or above) with the evolution of heat, but without decomposition or gaseous evolution. The optical activity disappeared during the reaction.

Weak acids, as oxalic, tartaric, and acetic, as well as zinc chloride and silicon tetrafluoride, were without action in the cold, although polymerization occurred to a greater or less extent at 100°C. in the presence of all but acetic acid and silicon tetrafluoride. The action of zinc chloride, slight at 100°C., was much more intense at 270°C., where pinene begins to be affected by heat alone. The course of the reaction was followed by the changes in density and optical rotation.

Heating at 100°C. in the presence of calcium, barium, and strontium chlorides, potassium cyanide, calcium fluoride, magnesia, sodium chloride, and mossy platinum caused no change, although at 200–240°C., where heat alone begins to have an effect, most of these substances did appear

to exhibit a catalytic influence. The chief product in each case was given the formula $C_{20}H_{32}$.

The product of the action of oxalic acid formed only a trace of artificial camphor on treatment with hydrochloric acid, and was not hydrated in the presence of nitric acid. The product of the action of zinc chloride at 100°C ., on the other hand, was readily hydrated. The action of zinc chloride also resulted in the evolution of hydrogen.

Carter, Smith, and Read (36) have recently found that both *d*- and *l*-pinene were readily polymerized to diterpenes in the presence of syrupy phosphoric acid. α - and γ -terpinene were formed simultaneously.

A similar observation was reported by Dehn and Jackson (40), who found that pinene and other terpenes were polymerized, and pinene was isomerized to dipentene and terpinene.

Turpentine gave a variety of products, among them colophene.

The polymerization of pinene with phosphoric acid has been discussed in the section on phellandrene, which behaved similarly.

Dulou (38) made a careful study of polymerization of the pinenes to give dipinenes. He catalyzed the reaction by acetic-sulfuric acid mixtures. From carefully purified α -pinene, obtained from Aleppo turpentine, he obtained a dipinene (" α -dipinene," b.p. 194°C . at 27 mm., d_{16} 0.930, n_D^{20} 1.5107, $(\alpha)_D$ 0, slightly viscous). On using β -pinene, obtained from Bordeaux turpentine, there resulted another dipinene (" β -dipinene," b.p. 174°C . at 17 mm., d_{20} 0.938, n_D^{20} 1.5177, $(\alpha)_D$ 0).

Both the bromine number and the Raman spectra indicated these two dipinenes to be mixtures of mono- and di-ethylenic hydrocarbons, with the monoethylenic compound being present in α -dipinene in the larger amount. Carter, Smith, and Read (36), on the other hand, found that the molecular refractivity of the diterpenes which they obtained by the action of phosphoric acid pointed to the presence of three double bonds. These authors, as well as Dulou, believed them to be dicyclic. The latter found that his α - and β -dipinenes were hydrogenated only to the extent of about 1 per cent in the presence of palladium or platinum black.

On dehydrogenation with sulfur, Dulou obtained a small amount of what he believed to be a diisopropyldiphenyl.

In devising a mechanism for the formation of dipinenes, Dulou applied the electronic theory of valence to the pinenes. He considered α - and β -pinenes to be conjugated systems, and formulated them thus:

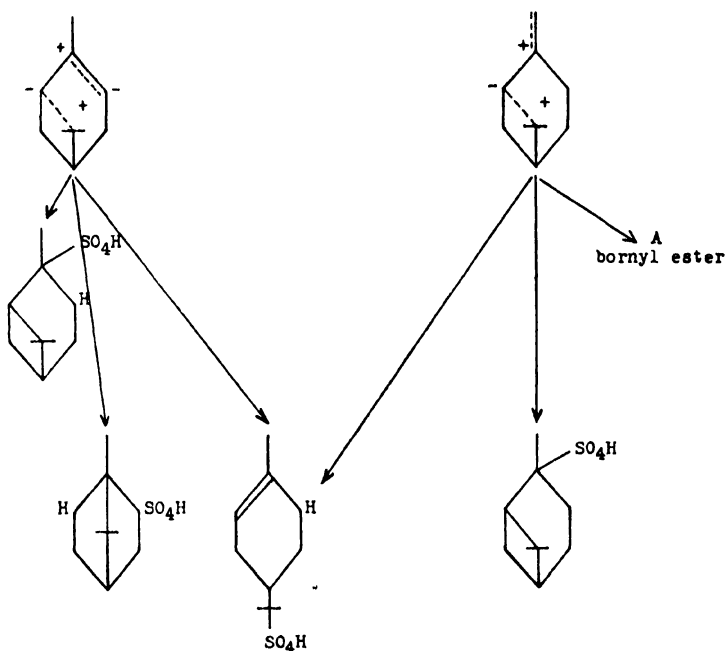


α -Pinene

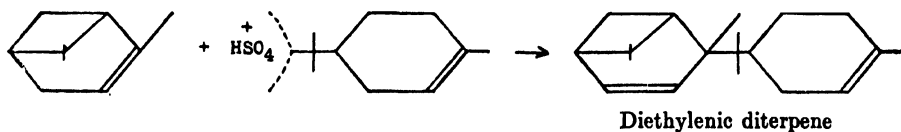
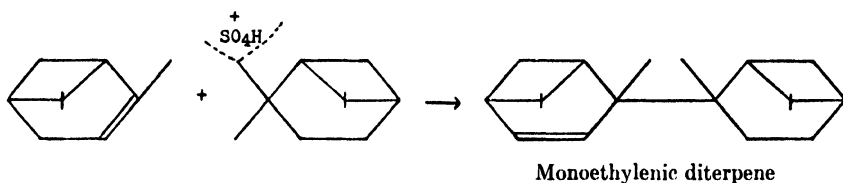


β -Pinene

They were believed to be polarized, and to possess the possibility of adding sulfuric acid as shown in the following scheme:



On this basis Dulou proposed the following mechanisms for the formation of mono- and di-ethylenic diterpenes:



The mechanism of Carter, Smith, and Read, previously described, was similar to that of Dulou in that both were based on the conjugated system existing in α - and β -pinenes. At that point, however, the two differed

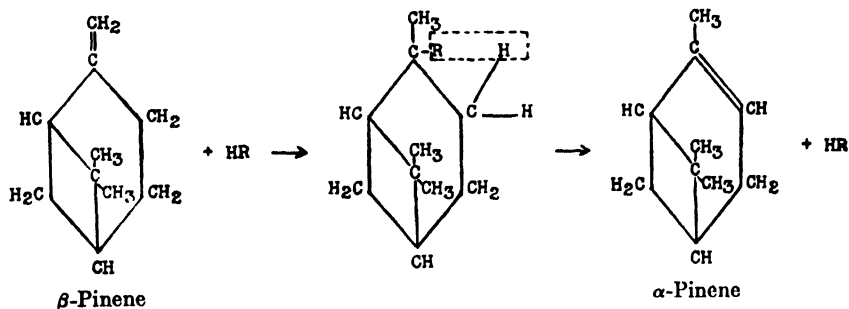
somewhat, in that that of the former postulated the addition and subsequent splitting out of water with the formation of triethylenic diterpenes.

Delepine (37) heated β -pinene with an approximately equal weight of benzoic acid at 150°C . for twenty to fifty hours, and found some α -pinene among the resulting esters and alcohols. By heating *l*- β -pinene with an excess of trichloroacetic acid at 60°C . there resulted a rapid transformation of a part of the β -pinene into α -pinene. He suggested that an ester might be intermediate in this reaction.

Austerweil (10) heated β -pinene with organic acids, e.g., two moles of salicylic acid with one mole of β -pinene at about 160°C . Besides a 35 to 36 per cent transformation into bornyl esters, he obtained a 1 per cent conversion to a mixture of α -pinene, limonene, and terpinene.

By using a weaker acid, as benzoic or abietic acid, at a temperature not exceeding 145°C ., α -pinene was the chief product. The weaker the acid, the less the quantity of bornyl esters produced. Thus when phenol was used, in the absence of water, only traces of bornyl and fenchyl esters were found, α -pinene being the only product.

The reaction was formulated as follows:



Aschan (7) gave a similar mechanism for the analogous action of hydrochloric acid on β -pinene.

On heating α -pinene for ten to twenty hours with an equal weight of benzoic acid at $125\text{--}130^{\circ}\text{C}$., Austerweil (11) obtained a very small quantity of limonene and 3 to 5 per cent of bornyl benzoate. Most of the α -pinene remained unchanged.

The addition of antimony trichloride in small amounts to *l*-pinene was found by Riban (123) to cause polymerization with the evolution of heat. The chief product was a transparent solid corresponding to the formula $\text{C}_{40}\text{H}_{64}$, and called tetrapinene (tétratérebenthène) as it was supposed to be a tetramer of *l*-pinene. It formed a monohydrochloride, a dihydrochloride, and a dihydrobromide, all amorphous.

The existence of colophene ($\text{C}_{20}\text{H}_{32}$) among the reaction products was also indicated.

On being heated above 350°C. the tetramer decomposed to simpler hydrocarbons; colophene, a hydrocarbon with a citrus-like odor, corresponding to the formula $C_{10}H_{16}$, called " β -isopinene," and a viscous substance of high boiling point, probably the "metapinene" of Berthelot.

The reaction of depolymerization was represented by Riban thus:



Genveresse (57) found that heating 1 kg. of pinene with 250 g. of crystalline arsenic acid just below the boiling point for half an hour resulted in an energetic reaction. The chief product was terpinene, along with terpineol. The transformation was explained on the basis of the hydration of pinene, followed by a dehydration of a part of the hydrate.

A recent patent (142) describes the catalytic conversion of α - or β -pinene to camphene by the use of water-soluble neutral sulfates that retain one molecule of water of crystallization up to 220°C. Among the examples cited, pinene is refluxed with $MgSO_4 \cdot H_2O$ to yield camphene. This catalyst may be replaced by the corresponding sulfates of zinc, iron, cobalt, nickel, etc.

Another patent (143) claims that acid catalysts, e.g., for the transformation of nopinene to pinene, or nopinene and pinene to camphene, are made more regular and of high efficiency by converting them to salts by means of bases and liberating them afresh from the salts. The catalysts are inorganic acids as titanitic, silicic, vanadic, arsenic, molybdic, antimonitic, or tungstic acids, complex acids such as borotungstic, tungstosilicic, stannophosphoric, boroacetic, or aluminoöxalic acids, or acid salts such as acid phosphates of magnesium, manganese, or vanadium.

(5) *Catalyzed by sulfuric acid.* Like other olefins one would expect the terpenes to form addition products with sulfuric acid, and this possibility is not excluded, but some interesting rearrangements and polymerizations have also been noted.

The first dipinene was prepared by Deville (39) in 1840. He obtained colophene by treating turpentine oil with sulfuric acid. No camphene was found, but rather an isomeric substance was formed during the reaction.

Bouchardat and Lafont (26) treated levorotatory turpentine oil with one-tenth its weight of sulfuric acid. The reaction mixture was then heated at 150°C. in an autoclave with an excess of alcoholic potash, giving camphene, terpinene, terpinolene, and polymers of those substances.

In some experiments on the hydration of pinene, Flavitski (50) found that when *l*-pinene was warmed with alcoholic sulfuric acid, an isomeric hydrocarbon appeared to be formed.

Armstrong and Tilden (1) obtained camphene from turpentine by the action of concentrated sulfuric acid. Wallach (187) interpreted this change as an addition of the acid to one of the double bonds and its subsequent splitting off, taking a hydrogen atom from a different position. Wallach obtained α -terpinene by heating α -pinene with concentrated sulfuric acid.

The rearrangement of *dl*- α -pinene to terpinolene when the former is shaken with half its volume of 50 per cent alcoholic sulfuric acid was reported by Henry and Paget (75).

The composition of the monoterpene fraction obtained by the treatment of turpentine with 50 per cent sulfuric acid at 80°C. has recently been studied by means of Raman spectra. Dupont and Gachard (43) have thus identified cymene, camphene, limonene, α -terpinene, γ -terpinene, terpinolene, and 1,4-cineole. In addition it was determined that four other substances, of unknown nature, were present.

Contrary to the opinion of other investigators, terpinolene was found to be present only in small amounts.

(6) *Catalyzed by adsorbents.* It has been observed by Gurwitch (59) that when pinene was mixed with 5 per cent of freshly dehydrated Florida earth, vigorous boiling occurred. A larger proportion of the earth might occasion the ejection of the whole of the liquid from the containing flask. Fractionation of the product of this reaction yielded 6 to 7 per cent of camphene and 37 per cent of sesqui- and poly-terpenes boiling above 200°C. No dipentene was found. No other adsorbents were found to cause polymerization, although a small amount of heat was generated by the action of blood charcoal or alumina.

More recently Venable (181) has studied the same reaction and finds that pinene yields no camphene. He attributes the camphene in Gurwitch's product to its presence in Russian turpentine oil from which Gurwitch probably obtained his pinene. Other products similar to those of Gurwitch were obtained, including a large amount of monoterpenes other than pinene, boiling from 160–185°C., and a polymeric fraction which begins to boil at 320°C.

Venable states that the dipinene, present in his high-boiling products (b.p. 320°C.), is almost always formed when a terpene is treated with active fuller's earth. This is the case not only with α -pinene but also with dipentene, terpinene, camphene, β -pinene, active limonene, and sabinene. Aromatic compounds such as *p*-cymene, however, are non-reactive. The reaction is not promoted by iron gel, silica gel, or activated charcoal.

In a paper published at about the same time as that of Venable, Gurwitch (60) reaffirmed the formation of camphene from pinene in the presence of floridin, and proceeded to discuss the mechanism of the transformation.

According to him, the rearrangement has three possible explanations; (1) the pinene molecule rearranges directly, without the formation of any intermediate, as a result of the direct catalytic action of floridin; (2) pinene combines with the water of hydration of floridin to give an alcohol, which then splits off water to give the isomeric hydrocarbon; (3) floridin first brings about, as the result of strong adsorption, a polymerization of pinene, analogous to that of amylene, which then, as a result of the liberated heat, is broken down to the isomeric terpenes. Such decompositions, with the formation of camphene, terpinene, and other monoterpenes, have been observed by Tilden and Armstrong (173) as a result of the distillation of polyterpene mixtures obtained in the treatment of pinene with concentrated sulfuric acid.

The reaction, itself, was violent unless both pinene and floridin were cooled before being mixed. At -20°C . it proceeded smoothly and slowly, hence Gurwitsch argued that the products of the rearrangement remained adsorbed on the surface of the catalyst. In confirmation, it was found that if the mixture was then allowed to come to room temperature, the action continued slow, being hindered by the adsorbed material. The slowing up of the reaction at low temperatures was not thought to be due to any lessened tendency for the reaction, itself, to occur, but rather to slower diffusion of the products of reaction from the surface of the catalyst. Conversely, without cooling, the reaction was violent because of the rapid diffusion from the surface of the catalyst, which became even more rapid with mounting temperature.

Besides isomeric monoterpenes, the action of floridin on pinene at low temperatures gave polymerization products. If one of the first two of the above explanations is correct, then these polymerization products are the result of secondary reactions, and the quantities of rearrangement products should be less than at higher temperatures. On the other hand, if the polyterpenes are intermediates in the rearrangement, in accordance with the third explanation, they must break down into isomeric monoterpenes as a result of thermal action. The reaction products should therefore be correspondingly richer in undecomposed polyterpenes at low temperatures. As shown in table 20, the latter was found to be the case.

All of these experiments were performed with catalysts selected from one lot of floridin with water content of 6.19 per cent. It is possible, however, to suppose that under the influence of various temperatures, the water content may have varied. The data in table 21 were collected by shaking the pinene and floridin, both at -20°C ., for half an hour, and then at room temperature for two and one-half hours.

The water content of the floridin also affected the intensity of the reaction started at room temperature, as shown in table 22.

A comparison of tables 21 and 22 shows that the intensity of the reaction decreases and the polyterpene content increases with increasing water content. If the rearrangement proceeds by addition and splitting-out of water, it would be expected that at low temperatures, where the reaction proceeds slowly, a part of the pinene, by addition of water, would on

TABLE 20

Polymerization of pinene in the presence of floridin

TEMPERATURE	UNCHANGED PINENE	POLYTERPENES IN UNCHANGED PINENE
<i>degrees C.</i>	<i>per cent</i>	<i>per cent</i>
About -20	About 0.6	>35
About -12	About 5.0	22
About 0	About 27	10.5
About 20	About 99	4.9

TABLE 21

Effect of water content on the polymerization of pinene

WATER CONTENT OF FLORIDIN	UNCHANGED PINENE	POLYTERPENES IN UNCHANGED PINENE
<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
6.19	99	4.9
8.1	67	7.1
10.0	11.2	20.1
11.83	1.2	30.0
18.2	0	- -

TABLE 22

Effect of water content of floridin on intensity of reaction in polymerization of pinene

WATER CONTENT OF FLORIDIN	INITIAL TEMPERATURE OF PINENE AND FLORIDIN	MAXIMUM TEMPERATURE ATTAINED IN REACTION
<i>per cent</i>	<i>degrees C.</i>	<i>degrees C.</i>
6.19	18	184
8.1	18.5	161
10.0	19	38
11.83	18	22
18.2	18.3	18.5

depolymerization result in the presence of some terpene alcohols. None were found, however.

Gurwitsch drew the following conclusions regarding the mechanism of the rearrangement: (1) the primary products of the action of floridin on pinene are polyterpenes; (2) isomeric monoterpenes are formed by the splitting of these polyterpenes by the heat of polymerization; (3) the

water of hydration of the floridin plays a part in the process; and (4) a source of the energy required for the polymerization of pinene is to be found in the physicochemical affinity between pinene and the strongly dehydrated floridin.

Further work in this field is that of Gallas and Montanes (51), who report that pinene gave no camphene on being heated to 150–200°C., with silex, active carbon, kieselguhr, or manganese oxide, but that dipentene was formed. Of course the formation of dipentene might be attributed to a simple conversion of pinene by heat. Mulcey (109) has obtained similar results from pinene using alumina.

While none of the above authors mentioned the formation of cymene or menthane by the action of fuller's earth, Humphrey (81) has been granted a patent for the production of *p*-cymene from pinene, dipentene, or other terpenes, using fuller's earth, kieselguhr, and related substances as catalysts. An example follows: "305 parts of terpene, boiling point 170–185°, are heated under reflux condenser with 75 parts of fuller's earth at a temperature of 170–200° for a period of 10 hours." About 125 parts of crude cymene are obtained from the residual oil by fractionation. The crude product contains *p*-menthane and a large proportion of polymerized terpenes as well as *p*-cymene. In fact, the patentee states that two-thirds of the terpene is converted to polymers, $(C_{10}H_{16})_x$, distilling above 300°C. Higher temperatures and pressures yield different proportions of cymene and menthane.

Carpmall (28) claimed that α -pinene "can be prepared by heating β -pinene or oils containing substantial quantities of β -pinene in the presence of catalysts comprising inert substances of porous structure, e.g., porous pot, "permutit," bleaching earths, fuller's earth, and similar porous substances which contain silicic acid in hydrated form."

The work on turpentine and pinene is summarized in tables 23 and 24.

2. Thujene

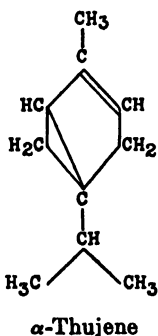


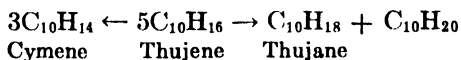
TABLE 23
Turpentine

REFERENCE NO.	TIME	TEMPERATURE	PRODUCTS	REMARKS
	<i>hours</i>	<i>degrees C.</i>		
(55)	—	"Heat"	More volatile than original; less volatile than original	
(14)	60	—	Little change	Refluxed in atmosphere of CO ₂
(14)	10	250	Polymerization products (iso- and meta-turpentine)	Closed tube
(14)	2	300	Isoturpentine	
(144)	—	—	"Colophonon," terpene	Dry distillation
(79)	—	Red hot tube	Gas, carbon, dark brown oil, C ₈ H ₈	Porcelain sticks in tube
(16)	—	Porcelain tube at moderate red heat	Benzene, toluene, xylene, cumolene, cymene, naphthalene	
(148)	—	Iron tube at dull red heat	Gas, benzene, toluene, <i>m</i> -xylene, naphthalene, anthracene, methylanthracene, phenanthrene	
(107)	—	—	Trimethylethylene and other products	
(77)	—	—	5.5 per cent yield of isoprene	
(146)	—	—	10 per cent yield of isoprene	
(99)	—	600	4.5 per cent yield of isoprene	Empty pyrex tube
		500	4.4 per cent yield of isoprene	Pyrex tube with porcelain
		550	2.5 per cent yield of isoprene	Pyrex tube with CuO and CuCl ₂
		450	5.0 per cent yield of isoprene	Iron tube—no contact material
(160)	—	Hot platinum coil	Small amount of isoprene	Vapors in high dilution with N ₂ or under 2-3 mm. pressure
(154)	—	550	Isoprene, benzene, toluene, xylene, no sesquiterpene or resin	Heating under 5-16 mm. pressure
(193)	—	—	Isoprene	Vapors mixed with N ₂ and passed through iron tube
(71)	—	750	27 per cent yield of isoprene	Steam used as diluent

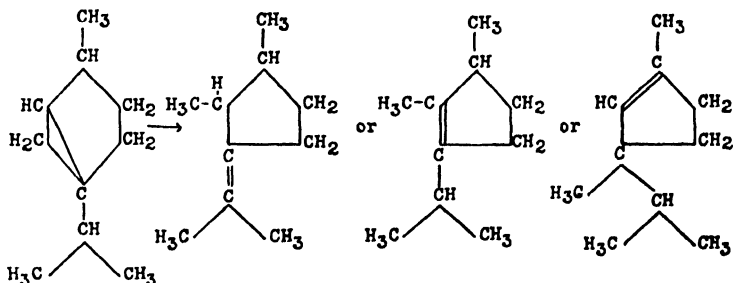
TABLE 23—*Concluded*

REFERENCE NO.	TIME	TEMPERATURE	PRODUCTS	REMARKS
	<i>hours</i>	<i>degrees C.</i>		
(72)	—	450–480	25 per cent yield of isoprene	Cu or Ag tubes or finely divided Cu or Ag in iron tube
(136)	—	350–360	A little benzene; abundance of cyclic and diethylenic hydrocarbons	Ni and stream of H ₂
(1)	—	—	Camphene	Concentrated H ₂ SO ₄
(108)	—	Dull red heat	Ethylene, propylene, butylene, divinyl, isoprene, trimethylethylene, benzene, toluene, xylene, olefins, and diolefins	Passed through a glass tube
(165)	—	0 and room temperature	Brittle polymer, (C ₁₀ H ₁₆) _x	AlCl ₃ added
	—	0 and room temperature	"Tough mass"	AlCl ₃ added with stirring
(165)			Paraffin and cycloparaffins, pentane, isopentane, trimethylethylmethane (?), octanaphthene, polynaphthenes, C _n H _{2n-2} and C _n H _{2n-4} hydrocarbons, dihydropinene (?), benzene, decanaphthene, high-boiling oil	Above "tough mass" heated
(124)	—	Room temperature	Paraffin, olefin, and naphthene hydrocarbons similar to petroleum	ZnCl ₂ , Al ₂ O ₃ + Cl ₂ , AlCl ₃ added
(40)	—	Room temperature	Variety of products, colophene	H ₃ PO ₄ added
(26)	—	Room temperature and 150	Camphene, terpinene, terpinolene, polymers	H ₂ SO ₄ added
(43)	—	80	Cymene, camphene, limonene, α -terpinene, γ -terpinene, terpinolene	50 per cent H ₂ SO ₄ ; analysis by means of Raman spectra
(39)	—	—	Colophene, hydrocarbon isomeric with camphene	H ₂ SO ₄ used

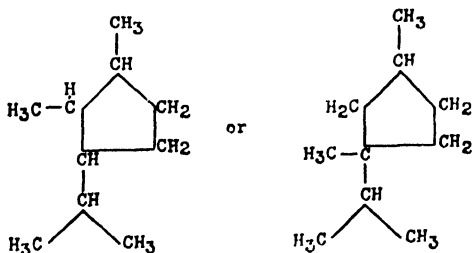
Catalytic decomposition. While no study of the non-catalytic pyrolysis of thujene has been found in the literature, Zelinsky and Kasansky (198) have reported that α -thujene, like pinene, undergoes irreversible catalysis in the presence of palladinized asbestos at 197–200°C. to form cymene, thujane ($C_{10}H_{18}$), and a hydrocarbon $C_{10}H_{20}$. The original hydrocarbon was passed over the catalyst in a quartz tube at the rate of four or five drops per minute. Zelinsky has written the reaction as follows:



Thujane (199) in a strong stream of carbon dioxide was passed over platinized charcoal. Instead of the expected cymene and hexamethylene compound, the product proved to be a pentamethylene compound which could not be dehydrogenated further. The reaction is represented as follows:



Hydrogenation. In an earlier study of thujene, Zelinsky (194) reduced it, in the presence of nickel, to a hydrocarbon $C_{10}H_{20}$. On the basis of its physical constants he suggested the following formulas for this compound. Kasansky (87a) has shown the first formula to be correct.



Tschougaeff and Fomin (174) pointed out that thujene adds only one molecule of hydrogen when reduced under pressure in the presence of platinum at room temperature. The product is a bicyclic dihydrothujene or thujane.

TABLE 24
Pinenes

REFERENCE NO.	TEMPERATURE <i>degrees C.</i>	CATALYST	PRODUCTS	REMARKS
(171)	Iron tube at dull red heat	—	Gas, acetylene, isoprene, benzene, <i>m</i> -xylene, cymene, carbon	Boiled in copper flask
(171)	Iron tube at bright red heat	—	Gas, benzene	
(65)	Glowing platinum wire	—	1 per cent yield of isoprene	
(77)	Glowing platinum wire	—	8 per cent yield of isoprene	
(146)	Glowing platinum wire	—	10 per cent yield of isoprene	
(120)	"High"	—	25 per cent isoprene, 17 per cent unidentified distillate, 44 per cent residue, 14 per cent gases	
(137)	500	Cu	Hydrogen, gaseous ethylenic hydrocarbons, 8 per cent liquid of b.p. <120°, 5.9 per cent liquid of b.p. 120–150°, 76.1 per cent liquid of b.p. 150–180°, 10 per cent liquid of b.p. >180°	More gases than above, benzene, toluene, isoprene, 1,3-pentadiene, amylene, hexene, ethylenic compounds, aromatics, cumene, cymene, methylbenzene, isomeric terpenes, condensed terpenes, olefins, diolefins, tarry residue
(137)	600–630	Cu		

(137)	600	Ni	Large amount of carbon, gas rich in H ₂ , little liquid	<p>β-Pinene used Vapors mixed with CO₂; α-pinene used Vapors mixed with CO₂; dihydropinene used instead of pinene Vapors mixed with CO₂; β-pinene used H₂ Vapors mixed with H₂ H₂ and <i>l</i>-α-pinene H₂ and <i>d</i>-α-pinene</p> <p>50 hours H₂</p> <p>α-Pinene used; concentrated H₂SO₄; 24 hours <i>dl</i>-α-Pinene shaken with 50 per cent alcoholic H₂SO₄</p> <p>Silex, active carbon, MnO₂, Kieselguhr</p>
(137)	600	Co	Results intermediate between those from Cu and Ni at 600°	
(166)	600	Fe	Like Ni causing intense charring	
(197)	500	—	Isoprene	
(197)	190-200	Pd-asbestos	<i>p</i> -Cymene, dihydropinene, methane	
(199)	300	Pd-asbestos	<i>p</i> -Cymene	
(200)	190	Pd-asbestos	<i>p</i> -Cymene, dihydropinene	
(136)	180	Ni	Dihydropinene	
(136)	350-360	Ni	Cymene, menthane	
(199)	195-200	Pd-asbestos	Dihydro derivative	
(199)	157-158	Pd-asbestos	Dihydropinene, but not same as above	
(184)	"Heat"	—	Limonene	<p>α-Terpinene</p> <p>Terpinolene</p> <p>Camphene, sesquiterpenes, polyterpenes (no dipentene) No camphene, monoterpenes, polymers, dipinene No camphene, dipentene</p>
(32)	200	—	Dipentene	
(195)	Room temperature	Palladium black	Isopinene	
(187)	100	—	α -Terpinene	
(75)	Room temperature	—	Terpinolene	
(59)	—	Florida earth	Camphene, sesquiterpenes, polyterpenes (no dipentene)	
(181)	—	Florida earth	No camphene, monoterpenes, polymers, dipinene	
(51)	150-200	—	No camphene, dipentene	

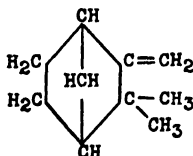
TABLE 24—*Concluded*

REFERENCE NO.	TEMPERATURE <i>degrees C.</i>	CATALYST	PRODUCTS	REMARKS
(109) (81)	— 170-200	Alumina —	Similar to above <i>p</i> -Cymene, <i>p</i> -menthane, polymers	Fuller's earth, kieselguhr, etc.; 10 hours α -Pinene used
(172) (17)	— Room temperature	Ni and Cu Electric discharge	Cymene, pinane Little change, slow polymerization to a diterpene	
(176)	Room temperature	Electric arc	Ethylene, acetylene, isoprene and other substances	
(122)	Room temperature	Pd + H ₂	α -Pinene, pinane	β -Pinene used on continued action
(15)	Room temperature	BF ₃	Dipinene	
	100	(COOH) ₂ Tartaric acid	A dipinene	
		ZnCl ₂	A dipinene	
		CaCl ₂ , BaCl ₂	A dipinene	
	200-240	SrCl ₂ , KCN	Slight effect	
		CaF ₂ , MgO	Slight effect	
		NaCl, Pt	Slight effect	
		H ₃ PO ₄	A dipinene, α - and γ -terpinene	Heat alone begins to be effective at this temperature
(36)	Room temperature			<i>d</i> - and <i>l</i> -pinene used
(40)	Room temperature	H ₃ PO ₄	A dipinene, dipentene, terpinene	
(38)	Room temperature	Acetic-sulfuric acid mixtures	α - and β -Dipinene	"Pinene and other terpenes" act thus
(37)	150 60	Benzoic acid Trichloroacetic acid	α -Pinene α -Pinene	β -Pinene used <i>l</i> - β -Pinene used

(10)	160	Salicyclic acid, limonene, terpinene	α -Pinene	β -Pinene used
(11)	145	Benzoic or abietic acid	α -Pinene	β -Pinene used
(123)	—	Phenol	α -Pinene	β -Pinene used
	125-130	Benzoic acid	Limonene	α -Pinene used
	Room temperature	SbCl ₃	C ₁₀ H ₁₄ hydrocarbon, colophene	L-Pinene used
(57)	"Heated"	Crystalline arsenic acid	Terpinene	
(142)	220	MgSO ₄ ·H ₂ O or analogous salts of Zn, Fe, Co, Ni, etc.	Camphene	
(143)	—	Titanic, vanadic, silicic, arsenic, molybdic, antimonie, or tungstic acids; borotungstic, tungstosilicic, stannophosphoric, borosilicic, or aluminooxalic acids; acetic, or aluminooxalic acids; acid salts as acid phosphates of Mg, Mn, or U	α -Pinene	β -Pinene used
(50)	"Warmed"	Alcoholic H ₂ SO ₄	Isomeric hydrocarbon	L-Pinene used
(60)	—	Floridin	Camphene	β -Pinene used
(28)	"Heated"	Porous pot, "permutit," fuller's earth, etc.	α -Pinene	

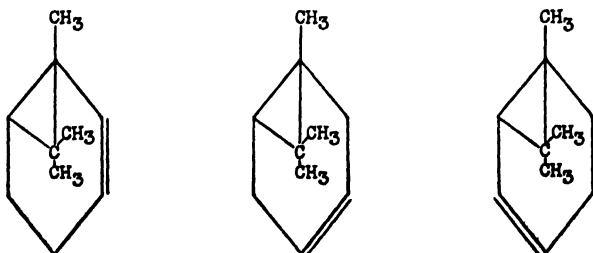
At a temperature of $155^{\circ}\text{C}.$, Zelinsky and Kasansky (198) reduced thujene, in the presence of palladinized asbestos, to form a hydrocarbon $\text{C}_{10}\text{H}_{20}$, the properties of which are very nearly the same as those of the product of reduction over nickel. Similarly, thujane ($\text{C}_{10}\text{H}_{18}$), when treated in the same way, yields a product which appears to be 1,2-dimethyl-3-isopropylpentane, but its identity with this known compound was not fully established.

3. Camphene



Camphene, which occurs in many natural oils (93), has been studied very little from the point of view of pyrolysis. Tilden (171) reported that its vapors when passed at atmospheric pressure through a glowing iron tube yielded "colophene." The term "colophene" has been used so differently by various investigators that it is safest to define it simply as a high-boiling polymerization product of terpenes.

By heating camphene with half its weight of phosphoric acid at $200^{\circ}\text{C}.$ for ten to twenty hours, Fujita (49) obtained a terpene, isomeric with carene, and a diterpene, closely related to thujane. The structure of the terpene was said to be one of the following:



When heated with a mixture of sulfur and phosphorus pentoxide, camphene yielded *p*-cymene.

Kuwata (92) has recently obtained a dicamphene (b.p. $318\text{--}321^{\circ}\text{C}.$) by stirring a benzene solution of camphene with Japanese acid clay for five hours. The yield of the crude dimer was 66 per cent.

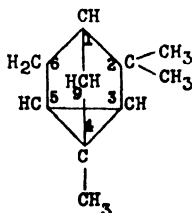
Staudinger and Klever (160) treated camphene, in high dilution with nitrogen under 2–3 mm. pressure, in a modified isoprene lamp and found that little or no isoprene was formed. What the products were, they did not state.

Simultaneous hydrogenation and dehydrogenation. In Sabatier and Gaudion's (136) work on simultaneous hydrogenation and dehydrogenation, which has been referred to previously, camphene was included in the group of terpenes studied. Camphene vapors mixed with hydrogen were directed onto a column of nickel at 350–360°C., with the result that the terpene was converted for the most part into cymene and cumene and only a small amount of a saturated hydrocarbon was obtained. These results are quite analogous to those obtained with limonene.

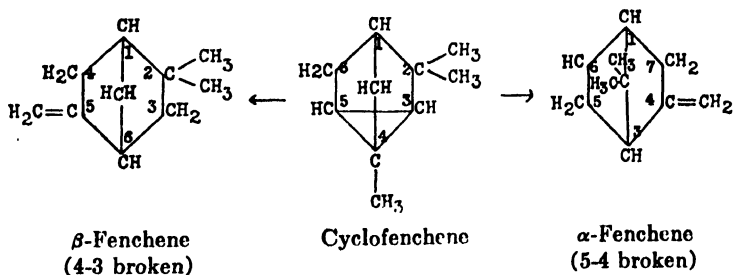
Hydrogenation. Some years previous to the above work, Sabatier and Senderens (138) had found that camphene yields a dihydro derivative, $C_{10}H_{18}$, when passed, with hydrogen, over nickel at 180°C.

D. TRICYCLIC TERPENES

1. Cyclofenchene



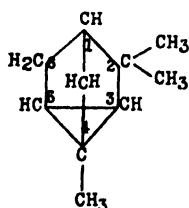
Catalytic decomposition. Zelinsky (199) has found that when cyclofenchene is passed over platinized charcoal at 300°C. it gives, in part, a mixture of α - and β -fenchene which arise from rupture of the trimethylene ring between carbon atoms 4 and 5 or 4 and 3.



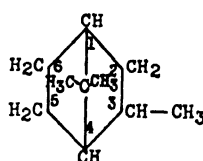
But Zelinsky states: "Tricyclic systems are not so easily broken as bicyclic so part of the original material is recovered. The fenchene obtained, like fenchane and isobornylane, is not dehydrogenated at 300°."

Hydrogenation. Zelinsky (199) has studied the hydrogenation of cyclofenchene over platinized charcoal, forming isobornylane at a temperature

of 155–160°C. The change, as shown below, involved the breaking of the trimethylene ring between carbon atoms 4 and 5.

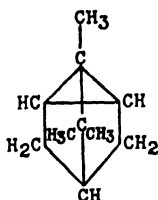


Cyclofenchene

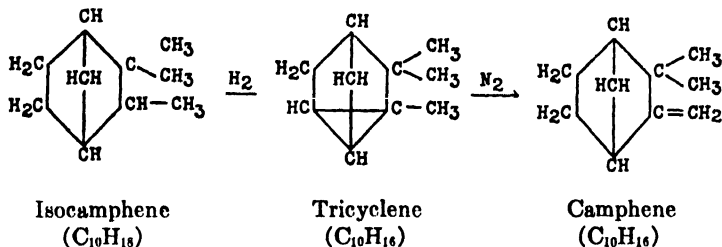


Isobornylene

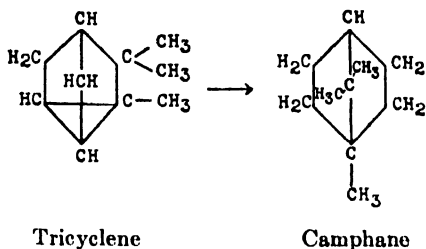
2. Tricyclene



Meerwein and Emster (102) have reported that tricyclene is converted to camphene in quantitative yield if it is passed over nickel at 180–200°C., the vapors being carried along by a slow stream of nitrogen. If the nitrogen is replaced by hydrogen, isocamphene is obtained. The reactions may be represented by the following equation, in which a rearranged formula for tricyclene is used in order to make the actual relation between the compounds a little more clear.



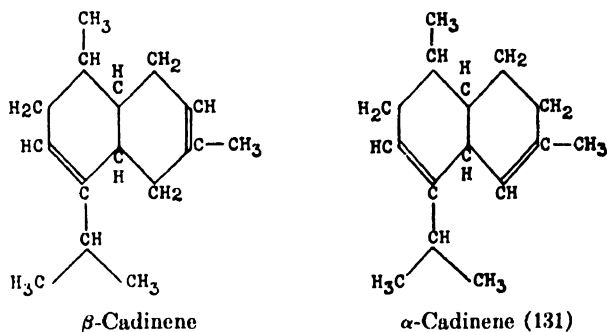
Platinized charcoal and hydrogen at 155–160°C., according to Zelinsky (199), cause the conversion of tricyclene to camphene. This is a result similar to those above, in that the trimethylene ring is broken, but in this case the break occurs between carbon atoms 4 and 5, while in Meerwein's work it was between carbon atoms 3 and 5.



V. SESQUITERPENES

The pyrolysis of sesquiterpenes is almost an unexplored field. This may be due to the fact that the sesquiterpenes are of complex and, until recent years, largely unproven structures. But probably a greater deterring factor is the difficulty of obtaining them in pure condition.

1. CADINENE



Cadinene appears to be quite stable, for Semmler and Jakubowitz (151) report that it is little changed even when heated for twelve hours at 330°C. in a bomb tube. The small amount of converted product appeared to be a monocyclic isomer of cadinene.

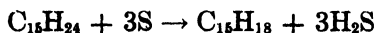
Lipishkin (97) has reported that when cadinene is heated in glacial acetic acid at 180–200°C., its rotation goes from -111.28° to -8° . The changes occurring were not investigated further.

Dehydrogenation

More recently Ruzicka and Stoll (131) have found that cadinene is dehydrogenated to cadalene, $C_{15}H_{18}$, when passed over platinum black and asbestos at 300–310°C. in a stream of inert gas such as nitrogen.

As stated previously, Ruzicka and his coworkers have dehydrogenated sesquiterpenes with sulfur. In this process the hydrocarbon is heated with three moles of powdered sulfur at temperatures ranging from 180–

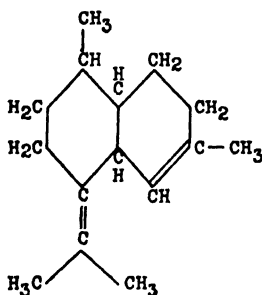
225°C. The reaction is complete within four or five hours and in some cases even less time is required. Ruzicka and Meyer (127) have written the equation



to represent the change that takes place in the case of compounds of the cadinene type.

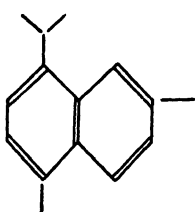
The first sesquiterpene (127) treated in this way was cadinene, from which cadalene, $\text{C}_{15}\text{H}_{18}$, was obtained. Shortly after this work was published, cadalene was proven (130) to be 1,6-dimethyl-4-isopropylnaphthalene. Calamene, zingiberene, and isozingiberene all behave like cadinene, yielding cadalene.

2. SESQUITERPENE FROM JAPANESE CEDAR OIL

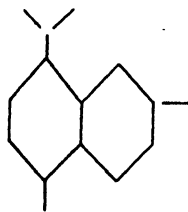


Catalytic decomposition

An unnamed sesquiterpene from Japanese cedar oil, according to Kimura (88), undergoes catalytic oxidation and reduction when heated to 280–300°C. for two hours in the presence of carbon dioxide and palladinized asbestos. The above structure has been proposed for this sesquiterpene, since this reaction yields decahydrocadalene and cadalene.



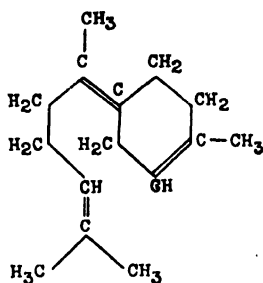
Cadalene



Decahydrocadalene

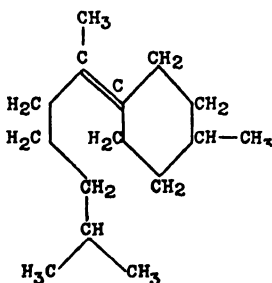
This work would indicate that the sesquiterpene is closely related to cadinene, but Kimura does not state that the two are isomeric.

3. BISABOLENE



Hydrogenation

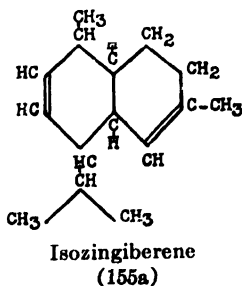
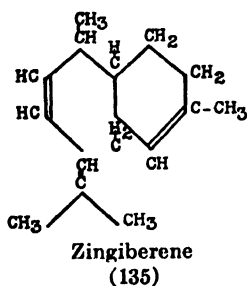
Bisabolene in cyclohexane solution may be hydrogenated to the tetrahydro derivative in the presence of platinum black at room temperature. Even at elevated temperatures Ruzicka and van Veen (135) have found that it does not add more than two molecules of hydrogen in this solvent. However, in glacial acetic acid the third molecule is absorbed quickly at room temperature. The suggested formula of the tetrahydro product is as follows:



Dehydrogenation by sulfur

Ruzicka and van Veen (135) heated bisabolene with two moles of sulfur and obtained a compound with a benzene ring, as proven by oxidation to terephthalic acid.

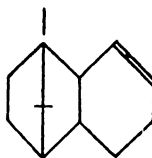
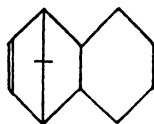
4. ZINGIBERENE



In Semmler and Becker's (149) work zingiberene was heated with isoprene for four hours in a bomb tube at 215°C. and yielded dipentene (probably from polymerization of isoprene); metazingiberene, boiling range 100–150°C. under 11 mm. pressure; a diterpene $C_{30}H_{48}$, boiling range 150–200°C. under 11 mm. pressure; and dizingiberene $C_{30}H_{48}$, boiling range 260–280°C. under 11 mm. pressure. By the addition and removal of hydrogen chloride and by heating with acetic-sulfuric acid at 60°C., isozingiberene, a dicyclic hydrocarbon, is obtained. The authors did not give a structure for metazingiberene. The proposed structures for zingiberene and isozingiberene are given above.

As already stated (127), zingiberene reacts with sulfur as does cadinene, yielding cadalene.

5. GURJUNENE



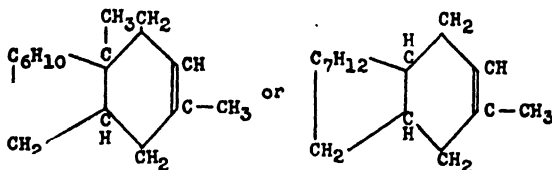
Ruzicka's cedrene type formula Semmler's cedrene type formula

Semmler and Jakubowitz (150) found that β -gurjunene (tricyclocedrene type) undergoes little change in properties when heated for four hours at 290°C. The only noteworthy change was that of rotation from $+27^\circ$ to $+60^\circ$, so the authors concluded that there could have been no decomposition. On the other hand α -gurjunene is completely inverted when treated under the same conditions.

In a more recent paper, Semmler and Jakubowitz (151) report that when heated to 330°C., β -gurjunene was converted to a brown, somewhat fluorescent oil yielding 12 per cent of a fraction consisting chiefly of α -terpinene with possibly small amounts of β -terpinene. The products also included unchanged β -gurjunene and a diterpene.

The α -gurjunene yielded an inactive terpene, $C_{10}H_{16}$, which is not terpinene, along with unchanged α -gurjunene and a diterpene.

6. CEDRENE

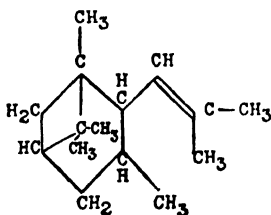


Ruzicka (134)

Cedrene has a great tendency to polymerize. Blumenn and Schulz (19) state that in the presence of acetic anhydride, or boiling under atmospheric pressure, it changes to a powdery, amorphous mass which regenerates the original cedrene when heated in vacuo.

When Semmler and Jakubowitz (151) treated cedrene as they did gurjunene, they obtained a terpene, $C_{10}H_{16}$, boiling range 65–70°C. under 10 mm. pressure; a fraction boiling between 90 and 130°C. under 10 mm. pressure (sesquiterpene); and a fraction boiling between 130 and 190°C. under 10 mm. pressure (diterpene).

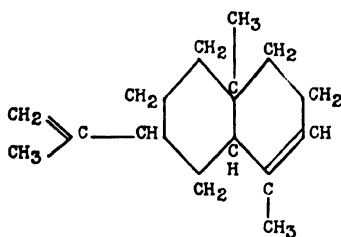
7. CARYOPHYLLENE



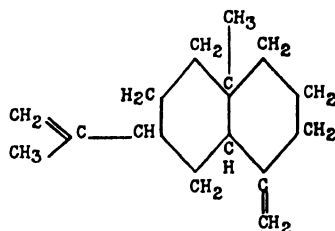
Ruzicka (128)

Caryophyllene (151), heated for twelve hours in a bomb tube at 330°C., yielded a terpene and a diterpene. The terpene was not pinene or limonene for it did not yield any crystalline derivative.

8. SELINENE



α -Selinene (130a)



β -Selinene (130a)

Ruzicka, Meyer, and Mingazzini (128) discovered that some sesquiterpenes lose a methyl group when dehydrogenated with sulfur. The reaction is represented as follows:



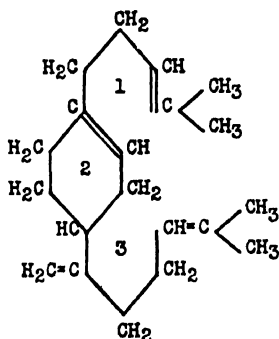
When selinene is treated in this manner it yields eudalene (129), 3-isopropyl-5-methylnaphthalene.

Table 25 summarizes the conditions of treatment and products obtained from the polymerization and decomposition of the sesquiterpenes.

TABLE 25
Sesquiterpenes

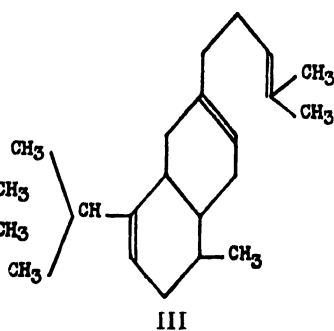
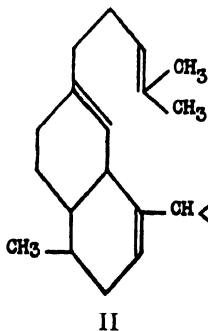
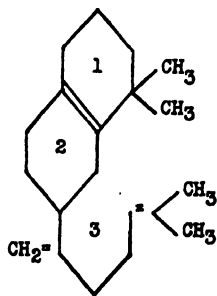
REFER- ENCE NO.	HYDROCARBON	TIME	TEMPERATURE degrees C.	CATALYST	PRODUCTS	REMARKS
(151)	Cadinene	12 hours	330	—	Monocyclic isomer or cadinene	Heated in bomb tube
(97)	Cadinene	—	180-200	—	Change of rotation from -111.28° to -8°	Heated in presence of glacial acetic acid
(131)	Cadinene	—	300-310	Platinum black	Cadalene (C ₁₅ H ₁₈)	Passed in stream of in- ert gas
(127)	Cadinene	4 or 5 hours	180-250	—	Cadalene (C ₁₅ H ₁₈)	Heated with sulfur
(88)	Sesquiterpene from Japanese cedar oil	2 hours	280-300	Pd-asbestos	Decahydrocadalene, cadalene	CO ₂ present
(135)	Bisabolene	—	Room tem- perature	Platinum black	Tetrahydrobisabolene	H ₂ in cyclohexane
(135)	Bisabolene	—	Room tem- perature	Platinum black	Hexahydrobisabolene	H ₂ in glacial acetic acid
(135)	Bisabolene	4 or 5 hours	180-250	—	Benzene derivative	Heated with sulfur
(149)	Zingiberene and isoprene	4 hours	215	—	Metazingiberene, diterpene, dizingiberene	Bomb tube
(149)	Zingiberene	—	60	HCl or acetic- sulfuric acid	Isozingiberene	—
(127)	Zingiberene	4 or 5 hours	180-250	—	Cadalene	Heated with sulfur
(150)	β -Gurjunene	4 hours	290	—	Change of rotation from +27° to +60°	—
(150)	α -Gurjunene	4 hours	290	—	Complete inversion	—
(151)	β -Gurjunene	—	330	—	12 per cent α -terpinene, β -ter- pinene, diterpene	—
(151)	α -Gurjunene	—	330	—	Inactive terpene, diterpene	—
(19)	Cedrene	—	Room tem- perature	—	Powdery amorphous mass	Acetic anhydride
(19)	Cedrene	—	At boiling point	—	Powdery amorphous mass	Atmospheric pressure
(151)	Cedrene	—	300	—	Terpene, sesquiterpene, diter- pene	—
(151)	Caryophyllene	12 hours	330	—	Terpene, diterpene	Bomb tube
(128)	Selinene	—	—	—	Eudalene, CH ₃ SH	Boiled with sulfur

VI. DITERPENES

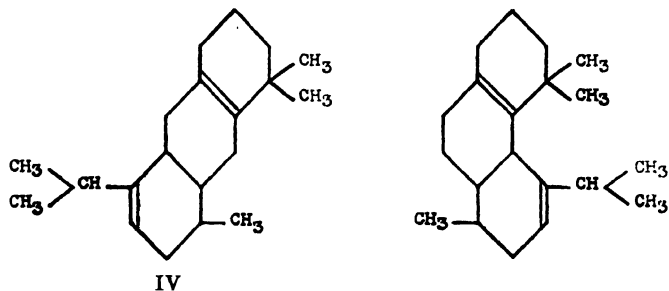
1. α -CAMPHORENE

The above formula for α -camphorene has been suggested by Ruzicka and Stoll (132).

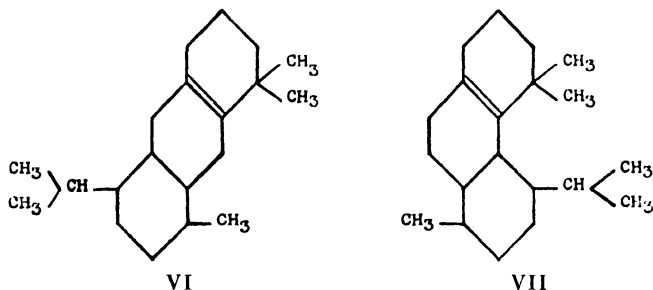
It was found by Semmler and Jonas (153) that heating with acetic-sulfuric acid mixtures caused the isomerization of α -camphorene to what they believed a bicyclic isomer which they called "iso- α -camphorene." Ruzicka and Stoll (132) obtained the same product by boiling α -camphorene for half an hour with two parts of 95 per cent formic acid. It boiled at 192–194°C. at 12 mm. The most probable formula for the bicyclic isomer was thought to be represented by I (below), although isomers represented by formulas II and III may also have been present.



On three hours further boiling, either of α -camphorene or the bicyclic product, with formic acid, a tricyclic isomer (b.p. 180–181°C. at 12 mm.) was obtained, for which formula IV was thought most probable, though the isomer represented by formula V was probably also present.



The tricyclic product was found to add only one mole of hydrogen in the presence of platinum black, forming a dihydro derivative of the formula VI or VII (b.p. 176°C. at 12 mm.).

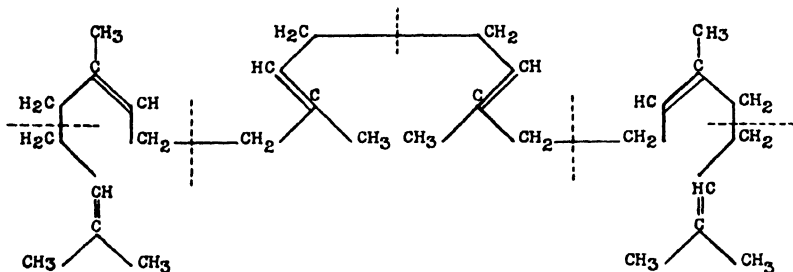


2. DACRENE

Blackie (18) has subjected dacrene, a naturally occurring diterpene of unknown structure, to cracking conditions with the hope that the results might aid in determining its structure. Eight grams of dacrene were gently distilled under 1 mm. pressure through a silica tube heated to 800–900°C. Decomposition occurred with the evolution of gas in such quantity that distillation was prevented until the “hyvac” pump could cope with the gases.

VII. TRITERPENES

SQUALENE



Squalene
Karrer and Helfenstein (85)

Considerable chemical and biological interest is attached to squalene, the dihydroterpene obtained from the unsaponifiable matter in the livers of elasmobranch fish, since metabolic processes in animals do not usually give rise to hydrocarbons. Though its biological significance is not well understood, it is suspected of having some connection with the origin of cholesterol.

Discovered in 1906 by Tsujimoto (175) and by him assigned the formula $C_{30}H_{50}$, its recent synthesis by Karrer and Helfenstein (85) indicates the above structure, which shows its relationship to the terpenes. It is seen to consist of six isoprene units.

The "spinacene" of Chapman (29) has been shown to be identical with squalene.

TABLE 26
Decomposition of squalene

BOILING POINT	PRESSURE	CONTENT	REMARKS
<i>degrees C.</i>	<i>mm.</i>	$\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3 - \text{C} = \text{CHCH}_3 \end{array}$	
30-45	760		No isoprene, as reported by Majima and Kubota (101)
60-100	20	Mono- and di-hydromonoterpenes	Under investigation
120-170	20	Mixture of monocyclic sesquiterpenes. Bisabolene identified	Cyclized by formic acid to dicyclic isomer
170-210	15	$C_{26}H_{42}$. Mixture of open chain and cyclic compounds	Oils, thought to be identical with compound obtained by Staudinger (164) on heating rubber ($C_{26}H_{40}$), were also present
210-240	15		Not investigated

Non-catalytic decomposition and polymerization

Heilbron, Kamm, and Owens (66) decomposed squalene by distillation at ordinary pressures. On fractionation of the product, the results shown in table 26 were obtained.

Abe and Shobayashi (3) found that when squalene was heated, it exhibited an exothermic reaction at about 185°C. This exothermic reaction increased suddenly at about 300°C. The data collected at 280-300°C. are given in table 27. Above about 355°C. the reaction became endothermic. These data were interpreted as meaning that in the cracking of squalene there is first a polymerization, followed by a decomposition of the unstable polymer to more volatile substances.

Oda (111) arrived at the same conclusion by heating squalene under 100 atmospheres of hydrogen. Heating for one hour at temperatures of 300–410°C. caused no change of pressure. At 450°C., however, the pressure increased rapidly to 260 atmospheres, and then fell off to 236 atmospheres at the end of one hour. The product had a boiling range of 39–260°C. (original b.p. 250–253°C.) and contained aliphatic hydrocarbons and terpenes.

Although heating at 300°C., with and without hydrogen pressure, caused the decomposition of squalene, it permitted polymerization to occur as a side reaction. The presence of hydrogen pressure appeared to cause depolymerization of a part of the polymer, with the result that in such experiments more of the unpolymerized hydrocarbon was present. Furthermore, the higher the temperature, the greater the quantity of low-boiling material, although no constant-boiling fractions appeared.

TABLE 27
Decomposition of squalene at 280–300°C.

TIME OF HEATING	IODINE NO. (Wjs)	MOLECULAR WEIGHT
<i>minutes</i>		
0	396.7	408.8
400	314.6	418.8
600	280.1	526.0
1045	247.1	555.4
1360	242.2	600.9
1700	227.5	747.7

Catalytic decomposition and isomerization

Chapman (30) decomposed squalene by distilling it at 45 mm. from a Wurtz flask, in the neck of which was suspended a platinum grid maintained at dull red heat. The gas which was produced consisted of 75 per cent of olefinic, and 25 per cent of paraffinic hydrocarbons. The liquid product was fractionated and contained considerable unchanged squalene. A small fraction (b.p. 40–50°C.) was thought to consist largely of isoprene and possibly some amylene. The chief product was a fraction boiling at 79–83°C. at 33 mm., or 160–167°C. at 750 mm., which corresponded closely to the formula $C_{10}H_{18}$. The bromine estimation indicated a mixture of mono- and di-ethylenic hydrocarbons, and a crystalline compound was isolated which corresponded closely to the formula $C_{10}H_{18}Br_4$. On being heated at its boiling point under atmospheric pressure, the hydrocarbon partially polymerized.

Heilbron, Owens, and Simpson (67) repeated the hot-wire decomposition

of squalene, but failed to confirm the existence of any individual substance. They obtained the same indefinite fractions as were found on direct pyrolytic decomposition. On boiling the monoterpene fraction from the hot-wire decomposition, there was produced a high-boiling hydrocarbon which closely resembled dimyrcene in its physical properties. They regarded this as evidence for the presence of an open chain hydrocarbon, perhaps myrcene, in that fraction.

Chapman (30, 31) found that squalene was also decomposed by distillation at 40–45 mm. over metallic sodium. The chief product was claimed to be a cyclodihydroterpene, $C_{10}H_{18}$, which added one mole of bromine, and was similar to cyclodihydromyrcene in its properties. It boiled at 170–175°C. at atmospheric pressure. This work was also repeated by Heilbron, Owens, and Simpson (67). Taking the fraction which Chapman found to be similar to cyclodihydromyrcene, they distilled it from a

TABLE 28
Cyclization of squalene

TIME	NO. OF DOUBLE BONDS	IODINE VALUE		$(R_L)_D$	NO. OF RINGS
		Calculated	Found		
<i>hours</i>					
$\frac{1}{2}$	—	—	—	136.9	2
3	3	185.8	179.9	134.3	3
9	3	—	—	134.1	3
24 (or more)	2	124.6	117.4	130.9	4

Willstätter flask and found it to boil at 162–177°C. On this basis, and after demonstrating that the evidence of bromine and iodine numbers could not be used, they concluded it to be a mixture of substances, rather than an individual compound.

Abe and Shobayashi (3) found that aluminum chloride favored the cracking of squalene, probably because it catalyzed the initial polymerization which was thought to occur.

When heated at ordinary pressure with Japanese acid clay, squalene was found by Kawai and Kobayashi (89) to give good yields of a mixture of hydrocarbons closely resembling natural petroleum. The mixture consisted chiefly of naphthenes, together with aromatic and unsaturated hydrocarbons.

The isomerization, or cyclization of squalene by certain catalysts was first discovered by Majima and Kubota (101), but they did not obtain a pure product. The best catalyst for this purpose is 98 per cent formic acid, and Heilbron, Kamm, and Owens (66) found that boiling with that

acid resulted in cyclization, the extent of which depended upon the time of boiling. Their results are shown in table 28. The viscosity increased with the number of rings produced, the final product being a treacle-like mass.

Distillation of the tetracyclosqualene caused decomposition and gave products similar to those obtained by the distillation of squalene itself. In addition, there was obtained a portion which resembled pinene in odor.

Harvey, Heilbron, and Kamm (70) noted that when squalene was cyclized with formic acid which had been previously used for that purpose, there was obtained a tetracyclosqualene whose physical properties differed slightly from that produced by fresh acid.

Catalytic hydrogenation and dehydrogenation

Chapman (29) found that squalene was completely hydrogenated at 200°C. by passing hydrogen through the liquid in which was suspended a platinum black catalyst. The product was a saturated paraffin hydrocarbon, $C_{30}H_{62}$, colorless, odorless, and slightly viscous, boiling at 280–281°C. at 24 mm.

At 150°C. in the presence of a nickel catalyst deposited on kieselguhr or cocoanut charcoal, Heilbron, Hilditch, and Kamm (68) found that the double bonds of squalene underwent selective hydrogenation, the six such bonds being hydrogenated consecutively until the saturated hydrocarbon was produced. Boiling with 98 per cent formic acid resulted in cyclization of the product of the absorption of one mole of hydrogen, and partial cyclization of the product of the absorption of two moles. The other products did not undergo this isomerization.

Harvey, Heilbron, and Kamm (70) found that squalene reacted explosively with sulfur, but that tetracyclosqualene reacted smoothly with a vigorous evolution of gas, and gave small quantities of an oil resembling *p*-cymene, and another substance later identified by Heilbron and Wilkinson (69) as 1,2,5-trimethylnaphthalene.

The berginization of squalene by Ormandy, Craven, Heilbron, and Chanon (112) gave a product resembling petroleum. It yielded 59.3 per cent of spirit boiling to 180°C., and 28.2 per cent of kerosene boiling to 300°C. The residue gave heavier oils and a benzene-soluble resin. Examination of the petroleum spirit fraction showed the following composition:

	<i>per cent</i>
Unsaturated hydrocarbons.....	6.8
Benzene.....	1.0
Toluene.....	5.1
Xylenes, etc.....	11.8
Open chain paraffins.....	49.7
Closed chain paraffins.....	25.6

TABLE 20

Squalene

REFER- ENCE NO.	TEMPERATURE	CATALYST	PRODUCTS	REMARKS
	<i>degrees C.</i>			
(66)	—	—	2-Methylpentene-2, bisabolene, mono- and dihydromonoterpenes, monocyclic sesquiterpenes, open and closed chain compounds, $C_{20}H_{32}$ hydrocarbon, oils	Distilled at ordinary pressure
(3)	150-400	—	Not isolated	Exothermic reaction to about 355°. Endothermic above 355°
(111)	300-450	—	Aliphatic hydrocarbons, terpenes, polymers	
(30)	Platinum grid at red heat	Pt	Olefinic and paraffinic gases, isoprene, amylene (?), $C_{10}H_{18}$ hydrocarbon, open chain	Distilled at 45 mm. through platinum grid
(31)	—	Na	Cyclic $C_{10}H_{18}$ hydrocarbon	Distilled at 40-45 mm. over sodium
(67)	Platinum grid at red heat	Pt	No definite product. An open chain hydrocarbon, perhaps myrcene (?)	Distilled at 45 mm. through platinum grid
	—	Na	No definite products identified	Distilled at 40-45 mm. over sodium
(3)	—	$AlCl_3$	Not isolated	Favored the cracking of squalene
(101)	—	Formic acid	Cyclic products	Boiled with formic acid
(66)	—	98 per cent formic acid	Di-, tri- and tetra-cyclo-squalene	
(89)	—	Japanese acid clay	Mixture of hydrocarbons resembling petroleum	
(29)	200	Pt	Saturated $C_{30}H_{52}$ hydrocarbon	Hydrogen present
(68)	150	Ni	Di-, tetra-, hexa-, octa-, deca-, and dodeca-hydro-squalene	Hydrogen present
(69, 70)	—	S	1,2,5-Trimethylnaphthalene	Tetracyclosqualene used
(112)	—	—	Petroleum containing unsaturated hydrocarbons, paraffins, benzene, toluene, xylenes, cycloparaffins. Isopentane, cyclohexane (?)	

Isopentane was identified, and there was evidence for the presence of cyclohexane.

The work on squalene is summarized in table 29.

VIII. RUBBER

Rubber, one of the most complex terpenes, has been the subject of pyrolytic investigation for almost a century. Bouchardat and Himley (25), in 1838, subjected rubber to dry distillation and obtained a hydrocarbon which boiled at 36°C., a "double hydrocarbon," and a mixture of less volatile hydrocarbons (b.p. about 315°C.) which they named heveene.

About ten years later Himley (78) was able to isolate from the products of pyrolytic decomposition of caoutchouc, two liquids, one of which boiled at 33–34°C., and the other at 168–171°C. The latter had the composition $C_{10}H_{16}$.

In 1860, Williams (192) found that the destructive distillation of rubber yielded a hydrocarbon boiling between 37 and 38°C. He found its formula to be C_8H_8 . That this compound, which he named isoprene, was not only a product of pyrolytic action but had the same empirical composition as rubber, was first established by Williams. He seems further to have regarded rubber as a polymeride of isoprene, for he states that the action of heat on caoutchouc is merely the disruption of a polymeric body into substances having a simple relationship to the parent hydrocarbon. Like Bouchardat, he also obtained heveene.

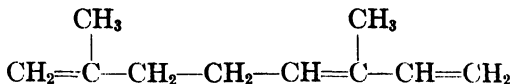
Bouchardat (23) carried out quantitative experiments on the pyrolytic decomposition of caoutchouc. By distilling 5 kg. of fresh para rubber, he obtained the following fractions: (1) about 40 liters of gas, chiefly carbon monoxide, some methane and about 10 g. of olefins; (2) 250 g. of isoprene; (3) 2000 g. of a hydrocarbon $C_{10}H_{16}$ boiling from 176–180°C.; and (4) 600 g. of a hydrocarbon boiling between 255 and 260°C., to which he gave the formula $C_{16}H_{24}$, and the name heveene, although the substance that he had previously called heveene boiled at about 315°C. The third fraction was inactive to polarized light and was called the dipentene fraction.

Bouchardat, like Williams, regarded caoutchouc as a hydrocarbon $(C_8H_8)_n$ which is decomposed by heat into a series of lower polymerides of the single hydrocarbon C_8H_8 . He considered that all the other distillation products were due in part to impurities and in part to the breaking-down of the products of oxidation of caoutchouc.

In addition to the products previously identified, Ipatieff and Wittorf (84) found trimethylethylene among the lower boiling products of destructive distillation of rubber.

In the so-called dipentene fraction, 2 kg. of which Bouchardat obtained

from 5 kg. of rubber, Harries (63) found that only one-third of the material was dipentene. From the mixture that remained after the removal of dipentene, he was able to isolate two other compounds, one of which he thought was possibly diisoprene.



In contrast to the results obtained by Bouchardat under atmospheric pressure are those of Fischer and Harries (47), who dry-distilled "para caoutchouc" under a pressure of 25 mm. They obtained very little isoprene and dipentene, the chief product being a mixture which boiled from 180 to 300°C.

Staudinger and Fritschi (158a) also studied the pyrolytic decomposition of rubber under reduced pressure. They used 340 g. of rubber, from which 4 to 5 per cent of resins had been extracted by means of a mixture of chloroform and methyl acetate. The distillation was carried out at 0.1–0.3 mm. pressure. From 216 g. of distillate they obtained 3.1 per cent isoprene; 8.8 per cent dipentene; 4.4 per cent $\text{C}_{16}\text{H}_{24}$, boiling from 88–91°C. under 0.05 mm. pressure; and about 4 per cent $\text{C}_{20}\text{H}_{32}$, boiling at 118–122°C. under 0.02 mm. pressure. No open chain terpene was detected. The sesquiterpene fraction contained a dicyclic compound with two double bonds.

In continuation of this work Staudinger and Geiger (159) found that when caoutchouc is heated to 300°C. under ordinary pressure, pyrolytic decomposition takes place; they obtained about 30 per cent of distillate, from which isoprene (about 40 per cent), pure dipentene, other sesquiterpenes, and higher terpenes were obtained. The residue formed a thick mass on cooling. About 20 per cent of high-boiling hydrocarbons were obtained from this residue by heating it under high vacuum. From this distillation there remained a dark brittle resin from which polycyclocaoutchouc was obtained almost quantitatively by solution in ether and precipitation with alcohol.

Geiger (56) states that the pyrolytic decomposition of rubber takes place in two steps. The first step begins at 290–300°C. in vacuo or 300–310°C. at ordinary pressures. The distillate from this step consists of isoprene, dipentene, and about 20 per cent of high-boiling oil. At the same time that this splitting occurs, there is an isomerization of part of the caoutchouc into the stable polycyclocaoutchouc, which forms in 80 to 90 per cent yield if the process is stopped after the first step. The second step begins at 335–345°C. and the distillate from this phase contains a little isoprene, no dipentene, and about 60 per cent of high-boiling oil.

Staudinger and Bondy (157) have found that the degradation of raw rubber appears to be inhibited somewhat, up to 142°C., by the presence of protein. At higher temperatures it follows a course similar to that observed with pure rubber.

The dry distillation of polycyclic caoutchouc was studied by Staudinger and Widmer (162). Under atmospheric pressure of carbon dioxide they found that decomposition begins at 350°C. and as the distillation proceeds, the temperature must be raised to about 450°C. In this way they were able to obtain a 92 per cent yield of volatile liquid decomposition products; about 3 per cent of a gas which was a mixture of methane and a small amount of unsaturated hydrocarbons; and about 5 per cent of a dark resin. From a fractionation of the distillate, at 13 mm. pressure, they obtained a minute amount of what may have been impure isoprene, a small amount of a fraction boiling at 111–113°C. which was a very unsaturated hydrocarbon having the composition of caoutchouc, and a fraction which had approximately the same boiling point as dipentene (174–176°C.) but different density and refractive index. The results obtained from the distillation of polycyclocaoutchouc under 1 mm. pressure were about the same as these, with the addition of a hydrocarbon the analysis and molecular weight of which indicated that it contained about seven isoprene units.

Another study of the destructive distillation of rubber is that made by Midgley and Henne (103). Two hundred pounds of light pale crepe rubber in 16-pound batches were destructively distilled at atmospheric pressure in an iron vessel connected to a suitable condensing system. No attention was paid to temperature control, because of the large size of the batches, but the temperature was always raised as quickly as possible to about 700°C. After removal of isoprene from the distillate by fractionation, the residual oil was subjected to thorough fractional distillation in a carborundum-coated spiral column.

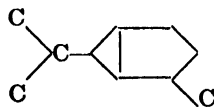
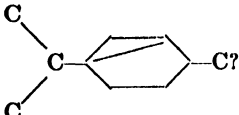
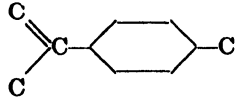
Briefly stated, the materials found in the distillate were olefinic, dienic, aromatic and hydroaromatic compounds, and a single dicyclic olefin. No fully saturated compound was detected. Table 30, taken from Midgley's paper, lists the compounds, the degree of accuracy of their identification, and the relative quantities present in the two types of distillates.

"In addition to the components which could be separated by fractional distillation, a substantial proportion of the original product polymerized, remaining as a jelly in the distilling flask. It may be safely assumed that the materials lost in this way consisted very largely of dienes which were too unstable to distill."

As the table indicates, the addition of magnesium to the rubber greatly increased the yield of materials other than isoprene and dipentene. The product is richer in compounds of the aromatic series and poorer in chain

compounds. Zinc, iron, brass, and aluminum have a similar effect, but to a very much smaller extent, while copper is without effect. Later they

TABLE 30
Compounds, identification and quantities

COMPOUNDS	DEGREE OF IDENTIFICATION	PER CENT IN DISTILLATE	
			With Mg
$C-C(C)-C=C$	Positive	0.04	0.2
$C=C(C)-C-C$	Positive	0.04	0.2
$C=C(C)-C=C$	Positive	10.0	10.0
$C-C(C)=C-C$	Positive	0.04	0.2
$C-C(C)=C-C-C ?$	Chain structure positive	0.06	0.30
$C-C-C(C)-C-C$	Positive	0.03	0.15
$C=C-C (C)=C-C$	Positive except for position of double bonds	0.03	0.15
Benzene	Positive	0.005	0.1
$C-C-C(C)=C-C-C$	Chain structure positive	0.03	0.15
$\Delta^3-C-C_6H_9$	Not positive	0.01	0.1
$\Delta^2-C-C_6H_9$	Suspected
$C-C=C-C-C-C(C)-C\Delta ?$	Chain structure positive	0.02	0.1
$\Delta^1-C-C_6H_9$	Positive	0.1	1.0
Toluene	Positive	0.05	1.0
$C-C-C-C-C-C(C)=C\Delta ?$	Chain structure positive	0.04	0.2
Dihydro- <i>m</i> -xylene	Positive	0.1	1.0
<i>m</i> -Xylene	Positive	0.05	1.0
$C-C-\text{C}_6\text{H}_4-C\Delta ?$	Positive	0.08	0.8
	Hydrogenation product		
		0.04	0.8
<i>p</i> -Methylethylbenzene	Positive	0.04	0.8
$C_{10}H_{18}$ (1 double bond).....		0.04	0.8
$C-C(C)=C-C-C-C(C)=C-C\Delta ?$	Not positive	0.015	0.0
	Positive	20.0	20.0
Total.....		30.87	39.05

(105) found that zinc oxide and magnesium oxide have an effect similar to zinc and magnesium, that of zinc oxide being by far the stronger.

"Because of the preponderance of isoprene (C_5), dipentene (C_{10}), and

heveene (C_{18}) in the products of destructive distillation, it is held certain that the single bond farthest removed from the double bonds is the most easily broken by pyrolysis. The same conclusion is arrived at by Hurd (82) from purely theoretical considerations and is found to hold when the other pyrolysis products are examined.

"It can scarcely be doubted that, with the exception of benzene, the compounds of the aromatic series were all derived by dehydrogenation of

TABLE 31
Compounds, identification and quantities

COMPOUNDS	DEGREE OF IDENTIFICATION	PER CENT IN DISTILLATE
Propylenes and butenes	Positive	0.3
$CH_3CH(CH_3)CH=CH_2$	Positive	0.2
$CH_2=C(CH_3)CH_2CH_3$	Positive	2.0
$CH_2=C(CH_3)CH=CH_2$	Positive	1.1
$CH_3C(CH_3)=CHCH_3$	Positive	4.2
Component boiling at 58°	Abridged	0.05
3-Methylpentenes	Positive	0.4
Component boiling at 68°	Abridged	0.1
Benzene	Positive	0.1
Isomeric heptane	Positive	0.03
Component boiling at 93-95°	Abridged	0.1
Tetrahydrotoluene	Positive	0.4
Toluene	Positive	0.1
Component boiling at 121-122°	Abridged	0.2
Hexahydroxylene	Possibly present	0.1
<i>o</i> -Xylene	Uncertain	0.006
<i>m</i> -Xylene	Positive	0.1
<i>p</i> -Xylene	Positive	0.02
Compounds with 9 carbon atoms	Similar to those from natural rubber but not investigated	0.5
Compounds with 10 carbon atoms	Similar to those from natural rubber but in too small amount to separate properly	6.4
Dipentene	Uncertain	0.1
Normal pentane, isopentane and dihydroxylene were absent		

the corresponding hydroaromatic forms, since only those aromatic compounds are formed whose hydro derivatives are also present. Dihydro-*m*-xylene is the only predictable ring compound in C_8 , hence, if dehydrogenation occurs, only *m*-xylene should result. If, on the other hand, *m*-xylene is a primary pyrolysis product, small amounts of the ortho and para derivatives, at least, should be present. Particular care was taken to ascertain that no other xylene was present than the meta derivative.

"The origin of benzene is obscure. It is not due to accidental contamination in the laboratory, since the presence of a metal in the rubber always

TABLE 32
Pyrolysis of rubber

REFERENCE NO.	TEMPERATURE	PRESSURE	PRODUCTS	REMARKS
	<i>degrees C.</i>			
(25)	—	Atmospheric	Hydrocarbon of b.p. 36°, "double hydrocarbon," heveene	
(78)	—	Atmospheric	Liquid, b.p. 33–34°, $C_{10}H_{16}$, b.p. 168–171°	
(192)	—	Atmospheric	Isoprene, b.p. 37–38°	
(23)	—	Atmospheric	Carbon monoxide, methane, olefins, isoprene, $C_{10}H_{16}$ (b.p. 176–180°), $C_{15}H_{24}$	
(84)	—	—	Above products, trimethyl-ethylene	
(63)	—	—	Diisoprene	
(47)	—	25 mm.	Isoprene, dipentene, mixture b.p. 180–300°	
(158a)	—	0.01–0.3 mm.	Isoprene, dipentene, $C_{15}H_{24}$, $C_{20}H_{32}$	
(159)	300	Atmospheric	Isoprene, dipentene, sesquiterpenes, higher terpenes, residue	
(159)	—	High vacuum	High-boiling hydrocarbons, resin containing polycyclocaoutchouc	Initial material was residue from above
(56)	290–300	"In vacuo"	Isoprene, dipentene, high-boiling oil, polycyclocaoutchouc	
(56)	300–310	Atmospheric	Same as above	
(56)	335–345	—	Isoprene, no dipentene, high-boiling oil	Initial material was residue from above
(162)	350–450	Atmospheric pressure of CO_2	Methane, gaseous unsaturated hydrocarbons, isoprene?, $(C_5H_8)_x$ of b.p. 111–113° under 13 mm. pressure, terpene b.p. 174–176°	Initial material was polycyclocaoutchouc

increases the amount of benzene in the distillate. Extreme pyrolysis in locally overheated spots might account for its formation."

In a more recent paper, Midgley, Henne, and Shepard (106) have studied

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METALLIC SALTS OF ALCOHOLS AND ALCOHOL ANALOGS

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I. INTRODUCTION

It is frequently said that chemical literature abounds in references to the preparation and properties of compounds which are as yet useless. Precisely the opposite is true of metallic salts of alcohols and their analogs, for, in spite of a long record of usefulness, they have rarely been studied for their own sake. Although they partake of the characteristics of both organic and inorganic compounds, their structural intricacies, limited to the organic anion, have only within recent years interested the organic chemist, while his inorganic fellow has never been eager to deal with salts containing hydrocarbon radicals. Moreover, the same reactivity that makes such compounds valuable in synthetic work renders them difficult to isolate and study.

The present discussion is designed to summarize existing knowledge

of the chemistry of these salts. It does not by any means purport to be a catalog of all literature references dealing with its title; to compile an exhaustive bibliography of the uses of sodium ethoxide alone would be an extremely formidable task. It is inevitable, therefore, that most details must be obtained by reference to the original sources. Every effort has been made, however, to avoid the omission of any general method of preparation or type reaction. In addition, tables have been constructed setting forth most of the known physical properties and many of the reactions of salts of alcohol types.

Practically all the compounds under discussion are derived from alcohols, amines, mercaptans, or hydrocarbons, i.e., from alcohols or their analogs in the ammonia, hydrogen sulfide, or methane systems, according to the ideas and nomenclature developed by Franklin (117). These views give additional significance to the marked chemical resemblance among such apparently unrelated compounds as $\text{Ca}(\text{OCH}_3)_2$, $\text{Na}_2\text{NC}_6\text{H}_5$, KSC_2H_5 , and NaCH_2CH_3 .

All such salts may evidently be represented by a general formula $\text{M}_x(\text{AR}_n)_y$. M represents any metal or highly electropositive radical;¹ A may be any polyvalent element; and R denotes hydrogen or any monovalent radical derived from the hydrogen compounds of the elements of Group IVB (C, Si, Ge, Sn, Pb).² The subscripts x, n, and y merely satisfy valence requirements. If every R is a hydrogen atom, the compound is not considered a salt of an alcohol type except in a formal way, like that in which water is called the simplest alcohol.

The nomenclature of these salts is reasonably uniform; usage has sanctioned the employment of such names as "metal alkyl oxide," "metal alkyl sulfide" (mercaptide), "metal alkyl amide," and "metal alkyl methide."³ The nomenclature recommended for organometallic compounds by the Committee on Nomenclature, Spelling and Pronunciation of the American Chemical Society (78) is admirable from an organic standpoint, but it quite obscures the polar nature of such compounds as possess this constitution. Despite its frequent occurrence, particularly in German

¹ For definitions see KRAUS: J. Am. Chem. Soc. **44**, 1217-39 (1922); **46**, 2196-2204 (1924).

² Kraus has suggested that the saturated hydrogen compounds of these elements be known collectively as hydranes.

³ The system of naming hydrocarbon radicals suggested by Vorländer (J. prakt. Chem. [2] **59**, 247 (1899)) and adopted in Bernthsen-Sudborough's "Textbook of Organic Chemistry" (D. van Nostrand Co., New York, 1931) is followed in this paper. "The term *alkyl* group comprises all such monovalent radicals, whether of the aliphatic series, e.g., CH_3 , C_2H_5 , or of the aromatic, e.g., C_6H_5 , $\text{CH}_2\cdot\text{C}_6\text{H}_4$, $\text{C}_6\text{H}_4\text{CH}_2$, etc. The purely aliphatic alkyl radicals are termed *aliphyl* groups, and the aromatic, *aryl*."

chemical literature, the term "alcoholate" applied to the salt of an alcohol (239a) is distinctly objectionable, since by analogy to "hydrate" (78) and "ammonate," it is used correctly only in referring to a salt containing alcohol of crystallization, like $\text{CaCl}_2 \cdot 2\text{C}_2\text{H}_5\text{OH}$.

A study of the frequency with which various elements or groups occur in described compounds reveals that the radical R is commonly derived from a saturated hydrocarbon. Substituted silicane (227), germane (219, 233, 218), or stannane (60) radicals, as in $\text{KGe}(\text{C}_2\text{H}_5)_3$ and $\text{NaNHSn}(\text{C}_6\text{H}_5)_3$, are rare, and lead derivatives of this kind are not yet known.

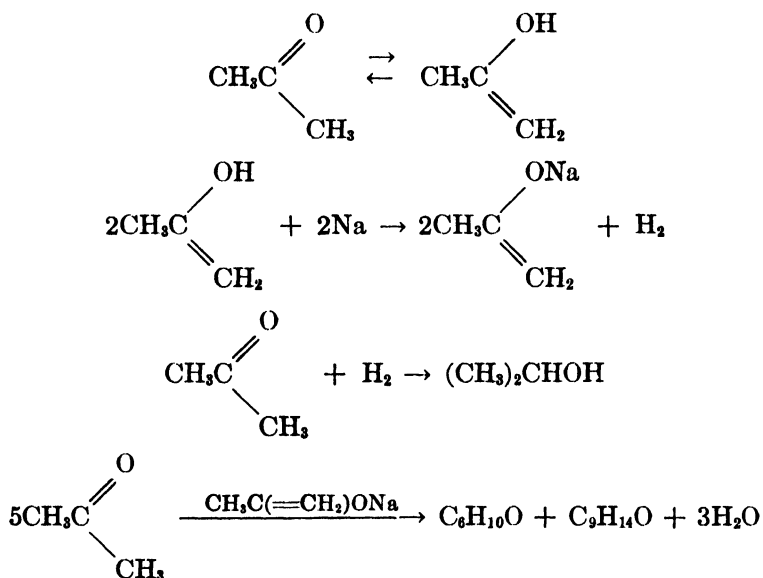
The nature of M is less limited. Metal alkyls have excited sufficient intrinsic interest so that investigators have succeeded in preparing members of the group representative of most of the common metals. The wealth of data on zinc dialkyls may even encourage a venture outside the realm of true salts, in the hope of bringing back ideas yet untried therein. The lack of spectacular properties in salts of amines, mercaptans (thiols), and alcohols has confined the study of these compounds almost entirely to those containing an alkali metal. Simple or alkylated ammonium groups and one tetraalkyl arsonium form (163) are the only positive radicals proved capable of yielding solid salts of alcohol types, although substituted phosphonium ethoxides (167) have been examined in solution. The only salts of other metals which have attracted more than casual attention are the alkoxides of aluminum, thallium, the alkaline earth metals, and zinc; the aryl amides of calcium and zinc; and some mercaptides of the heavy metals.

The variation of the middle element A is restricted to Subgroups B of Groups IV, V, and VI. Oxygen, carbon, or sulfur most frequently occupies this central position, although nitrogen derivatives are attaining increased familiarity. Salts containing selenium, tellurium, phosphorus, arsenic, or antimony have been partially or wholly neglected because of the disagreeable and poisonous nature of the parent substances, although Job and his coworkers (194, 195, 193) have demonstrated the possibility of establishing such metal-element linkages by securing the mixed compounds $\text{C}_6\text{H}_5\text{P}(\text{MgBr})_2$ and $\text{C}_6\text{H}_5\text{As}(\text{MgBr})_2$. Largely through the efforts of Kraus, four other elements—silicon (213, 217, 227), germanium (219, 233, 216, 218, 230), tin (220, 229, 225, 226), and lead (114)—have been shown to form salts of the type NaAR_3 in liquid ammonia or amines. The formally similar compounds of boron (234, 236, 235, 28), aluminum (237), and gallium (231), which constitute the only instances in which an element outside Groups IV, V, and VI enters such a combination, are probably abnormal in electron configuration. No doubt atoms of elements of Groups II and III already carrying alkyl radicals are incapable of combining with other metals, for Kraus and Kurtz (224) were unable to

prepare NaHgC_6H_5 by reducing phenylmercuric chloride, $\text{C}_6\text{H}_5\text{HgCl}$, with sodium.

II. PREPARATION BY OXIDATION-REDUCTION REACTIONS

A widely used method for preparing salts of alcohol types involves the reduction of some part of an organic molecule, usually by a metal. Since the latter must supply electrons with some facility, sodium and potassium are most important in this rôle. The organic material may be volatilized and passed over the heated metal, or the reaction may be realized in solution. In an undiluted compound, the presence of an alkali metal and the heat of reaction often lead to rearrangements and polymerization, while any nascent hydrogen is likely to produce undesirable reduction, as it does in the action of sodium upon acetone.



Of the various solvents (liquid ammonia, ethers, hydrocarbons) capable of moderating the former of these effects, liquid ammonia is by far the best. Its capacity for dissolving metals unchanged makes possible a homogeneous reaction of controllable speed, while its slight tendency toward autoionization precludes destructive ammonolysis of nearly all salts of alcohol types except the more reactive metal alkyls and their silicon analogs, e.g., NaC_2H_5 , KC_6H_5 , and $\text{NaSi}(\text{C}_2\text{H}_5)_3$.

1. The action of organic acids on metals

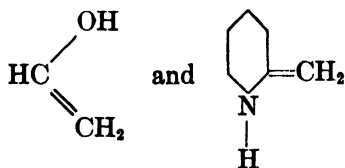
The action of a metal on an alcohol or an alcohol analog exemplifies a familiar kind of oxidation-reduction,—the displacement of hydrogen

from an acid by a metal (408). This historically important reaction was first applied by Liebig (251) to the preparation of sodium ethoxide, and was subsequently of service to Gladstone and Tribe (138), who first obtained aluminum alkoxides.



The metal or an alloy is caused to react with the pure or dissolved alcohol type, various catalysts (iodine, stannic chloride, nitrobenzene, boron trioxide, or almost any compound of a heavy metal) sometimes being valuable accelerators. The reaction velocity diminishes progressively as the number and molecular weight of hydrocarbon groups attached to the central atom increases, and decreases also when the organic compound contains moisture (347).

For a given metal, the extent of reaction with different alcohol types depends largely upon the acidities of the latter, which vary with their structure. The acidities of corresponding acids in different systems of compounds are qualitatively related to each other as the acidities of the parent substances are related; these assume the order (acidity of) $\text{H}_2\text{S} > \text{H}_2\text{O} > \text{NH}_3 > \text{CH}_4$. Within a system, the nature and number of R groups in the compound $\text{M}_x(\text{AR}_n)_y$ have a decided influence. Aryl radicals linked to the central element A produce more acidity than aliphyl radicals. The ionizability of hydrogen attached to A is also enhanced by an increased number of aryl groups similarly bound to that element, as is illustrated by the relative acidities of methane, toluene, diphenylmethane, and triphenylmethane. On the other hand, the escaping tendency of the proton seems to vary inversely as the number of alkyl radicals substituent on the main carbon or other atom of an R group; thus primary alcohols are stronger acids than secondary ones, which in turn surpass the tertiary forms. Because of the double bond in the R group, the acidity of enolic forms of monoaldehydes and monoketones and their analogs, like



is probably rather high. It is difficult to verify this by measuring the rate at which these compounds react with metals, since, although the equilibrated mixture of tautomers may be practically devoid of the enol (acidic) form, the tautomeric shift will replenish the decreasing supply of that form. When several hydrogen atoms are linked to the same central atom, as in aniline or methane, the replacement of one hydrogen atom by

metal invariably diminishes the acidity of the compound materially. This accords with the observation that salts in which the molecule contains more than one atom of even an alkali metal are extremely rare.

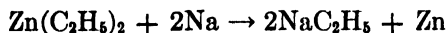
Aluminum, the alkali metals, and to a smaller extent those of the alkaline earth family, react more or less with all alcohols, mercaptans, and aromatic amines, although Kirner (208) has observed an anomalous failure of cold methyl mercaptan to attack sodium unless the relatively weaker acid, ethyl alcohol, is present. A semi-commercial process (49) for making sodium phenylamide by this method employs either excess aniline or a high-boiling hydrocarbon as solvent, and cuprous oxide, nickelous oxide, or cobaltous oxide as a catalyst (89) to reduce the temperature required. The action of cesium on liquid aliphatic amines (308), of calcium on aromatic amines (103), and of magnesium on alcohols is normal, but the instability of the salts toward heat renders the vapor method inapplicable to their preparation. That this limitation is not insurmountable is attested by Titherley's (384) preparation of potassium ethylamide from the gaseous amine, and Terentiev's (372) success in similarly securing magnesium aryl amides.

Only those hydrocarbons and analogs containing especially active hydrogen atoms (fluorene, triphenylmethane, triphenylstannane) are known to react as acids with alkali metals. It has been suggested, however, that under appropriate experimental conditions cesium may displace hydrogen from even alkanes (262).

The reaction of the highly electropositive metals with the more acidic hydrocarbons (76, 245), monohydric alcohols (59, 232, 414, 364), polyhydric alcohols (337), aromatic amines (302, 412), and pyrroles (116) is facilitated by dissolving the metals in liquid ammonia.

2. The reaction of metals with salts of alcohol types

The extent to which one metal displaces another from salts is governed by the relative positions of the two in the electrochemical series, if other variables are neglected. Since most salts of highly electropositive metals are more readily obtained by other means, such a process loses in importance as a preparative method. Another metal may displace zinc or mercury from an ester-like alkyl,



but not infrequently, as in the case represented, the new metal alkyl cannot be isolated from the reaction mixture except as a double compound (402, 143). Lithium reacts with Grignard reagents in ether,



but the slowness of the displacement usually renders decomposition of the lithium alkyl by the ether unavoidable (330).

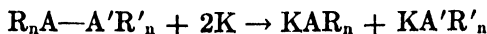
3. *Direct combination of metals and free radicals*

The mechanism of the displacements already discussed is believed by many authorities to include the action of the metal on free radicals. Even when this controversial point is disregarded, reactions may be found in which preëxistent radicals participate. Repeated corroborations of the discovery, by Paneth and his students (296, 297), that free aliphyl groups can exist in a gas and can combine directly with metals, excite the thought that true salts of hydrocarbons should be so obtainable. Full confirmation of this prediction has been supplied by Simons and Dull (352), who have prepared sodium methyl and sodium ethyl by just such a method. Alkali metals are similarly attacked by free groups in ethereal solution (427), although triphenylmethyl yields only polymeric derivatives unless a metal amalgam or solution is employed (335). The monomolecular radicals R_2Ge , R_2Sn , and R_3Sn , while insoluble in liquid ammonia, react smoothly with a metal dissolved therein (220, 229, 216).

When a solution containing a salt of an alcohol type is electrolyzed, almost any metallic anode, unless it consists of a noble metal, is converted into the corresponding salt. Such disintegrations of the positive electrode have been observed in the electrolysis of sodium alkyls dissolved in zinc diethyl (158, 159), of Grignard reagents in diethyl ether (120), and of sodium alkoxides in alcohols (370, 369). The possibility exists, of course, that the reactivity responsible for the change is to be assigned to the anions themselves (427) rather than to the free groups resulting from their discharge.

4. *Reduction of other organic compounds by metals*

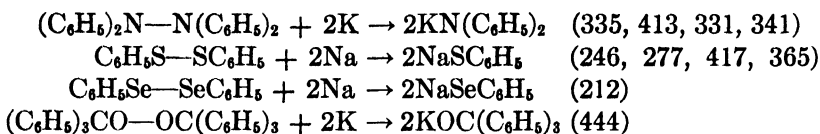
For some time after the discovery of the dissociation of hexaphenyl-ethane, metallic potassium was used to estimate the magnitude of such dissociation in related hydrocarbons by removing the free radicals. It has since been shown that the degree of reactivity of a hydrocarbon toward a metal can indicate only the relative instability of the central bond; the alkali metals are now known to cleave undissociated molecules.



Many compounds in which A and A' are atoms of the same Group IV element fail to react unless the metal is dissolved in liquid ammonia, in which medium insolubility of most metals and ammonolysis of the products restrict the usefulness of the method. In general the carbon-carbon bond proves too stable to be broken unless each atom carries several aryl

groups, as in $(\text{C}_6\text{H}_5)_2\text{CH}-\text{CH}(\text{C}_6\text{H}_5)_2$ and other polyphenylethanes (421, 71, 12). The silicon-silicon bond cannot be severed at all (213, 227), but sodium in liquid ammonia accomplishes normal reductions of germanium (219, 216, 218, 230) and tin (213) compounds of this type. However, the truth of the original report (413) that azobenzene can thus be cleaved to disodium phenylamide is doubtful (214).

To emphasize the extensive applicability of this kind of reduction, the following equations illustrating its occurrence are cited:



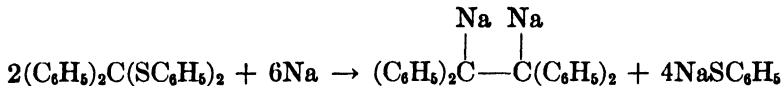
There has recently been reported (43) the cleavage of tetraphenyldiarsyl, $(\text{C}_6\text{H}_5)_2\text{As}-\text{As}(\text{C}_6\text{H}_5)_2$, by sodium-potassium alloy, but the resulting salt, the first representative of its type, was not isolated or studied except in its reaction with bromobenzene to yield triphenylarsine. It would be of interest to attempt a similar cleavage of cacodyl, $(\text{CH}_3)_2\text{As}-\text{As}(\text{CH}_3)_2$.

The reduction of diphenyl disulfide as expressed by the equation (248)

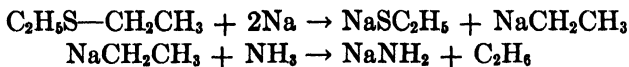


may also be accomplished by other metals, including zinc and lead (293, 419, 246).

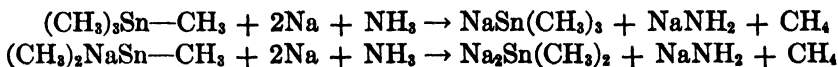
When the two central atoms are dissimilar and one of them is carbon, the stability of the connecting bond can scarcely be predicted. Neither $(\text{C}_2\text{H}_5)_3\text{SiC}_6\text{H}_5$ nor $(\text{C}_2\text{H}_5)_3\text{SiCH}_2\text{C}_6\text{H}_5$, the only tetraalkylsilicanes yet tested, undergoes cleavage by sodium in liquid ammonia (227). On the other hand, sodium splits dialkyl sulfides (343) and thioacetals (339),



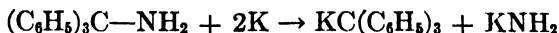
although in liquid ammonia (232, 417) the metal alkyl ammonolyzes.



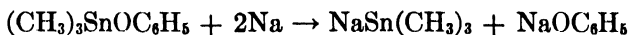
Tetraarylgermanes (219) and tetraalkylstannanes (229, 60) in the same solvent are cleaved by sodium, perhaps repeatedly.



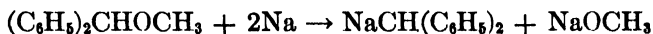
Triphenylmethylamine is so weak an acid that its reaction with metallic potassium in liquid ammonia gives, not the expected salt, $(C_6H_5)_3CNHK$, but cleavage products (228).



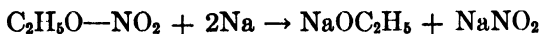
The ammono ether, trimethylamine, reacts with cesium at ordinary temperatures, but the reaction has not yet been studied (87). Aquo ethers are unaffected by sodium in liquid ammonia (232), unless one or both of the R groups is a stannyl or a germanyl radical, as in $(CH_3)_3SnOC_6H_5$ or $[(C_6H_5)_3Ge]_2O$ (219, 226, 218).



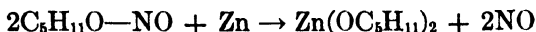
Schorigin (342, 343) found that high-boiling aromatic ethers react at their boiling points with either sodium or sodium-potassium alloy; those having smaller molecular weights and lower boiling points require long heating with the metal in a sealed tube. At 200°C. aliphatic ethers of low molecular weight resist decomposition by an alkali metal alloy over extended periods (164), and even metallic cesium does not cleave diethyl ether at room temperature (87). In spite of the tendency of the new metal alkyl to decompose by reacting with unchanged ether or side-products of the reaction (2), Ziegler (444, 443) and others (69, 341, 340, 29a) make use of the Schorigin cleavage of aromatic ethers to obtain alkali metal salts of hydrocarbons.



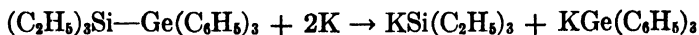
Almost no information is at hand relative to the stability of linkages in which carbon does not participate. Some early work of Chapman and Smith (58) indicates that aliphyl nitrates are split normally by sodium,



and that aliphyl nitrites undergo a similar cleavage by zinc,



but react with sodium in a more complicated manner. More modern investigators (227, 217) report the splitting of the mixed hydranes $(C_2H_5)_3Si-Ge(C_6H_5)_3$ and $(C_6H_5)_3Si-Sn(CH_3)_3$,



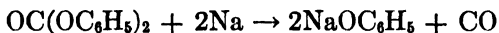
by which the difficultly accessible silicon salts are obtained.

The breaking by sodium of the titanium-oxygen bond in tetraethyl

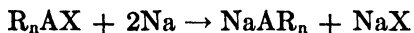
titanate (256) belongs to the rare type in which both fragments are not salts of the metal employed.



The complex decomposition of some carboxylic esters by the same metal (130, 119, 300, 45) involves a related scission of a carbon-oxygen bond, the primary reaction being of the type



The reducing power of the alkali metals is equally competent to transform many halogen compounds into salts.



Triaryl halides of carbon (335, 223, 143) and tin (220, 225) are most frequently subjected to this reduction, although lithium reacts very well with practically all alkyl halides (440, 438, 133, 422, 137, 71). Metals outside Group IA, if they have any effect, usually yield mixed salts of the Grignard type, XMAR_n ; but it is now generally admitted that the Grignard reagent exists as an equilibrium mixture.



While phenylmercaptomercuric chloride cannot be prepared directly from the metal, its disproportionation is similar (247).



Reductions of the type $\text{R}_n\text{AX} + 2\text{Na}$ remain undemonstrated for halides belonging to other than hydrane systems, chiefly because the excessive instability of such halogen derivatives (R_2NCl , ROCl , RSCl) renders their study difficult.

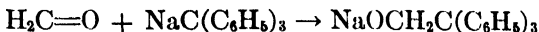
5. Reductions by means of salts of alcohol types

Much of the reducing potency of the metals is transmitted to their salts of alcohol types, as the recognized tendency of the latter to undergo oxidation shows. Ordinarily molecular oxygen causes complete disintegration, but in several tin (60) and germanium (219) compounds an irreversible conversion of a salt belonging to a hydrane system into an alkoxide is effected.

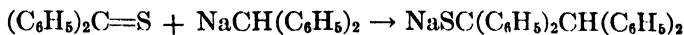


A related change is the addition of metal alkyls to various types of unsaturated linkages. Provided that no enolic form can be present to react as an acid, this addition may produce new salts of alcohol types. Under

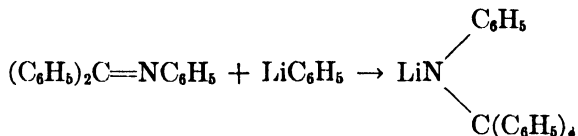
these conditions some aldehydes and ketones give alkoxides (336, 332, 133, 29a),



thioketones produce mercaptides (30),



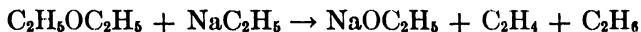
ammono ketones yield alkyl amides (446, 432, 134),



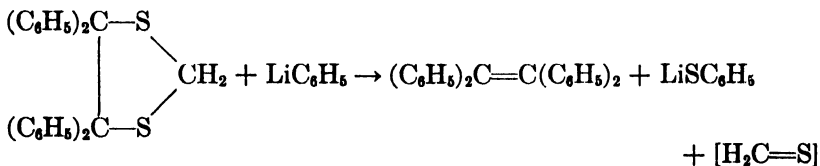
and some ethylenes form salts of other hydrocarbons (439, 431, 134).



It is of purely theoretical interest to note that metal alkyls decompose ethers (2) and organic disulfides and diselenides (341), although not dialkyl sulfides (124).



Lithium phenyl breaks a carbon-sulfur bond in its reaction with a few cyclic sulfur compounds (338).

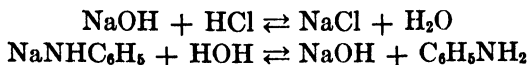


One sulfur atom in aromatic disulfides is likewise reduced by potassium diphenylamide (341), and even by some salts of thiols (249).

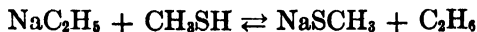
III. PREPARATION BY METATHETIC REACTIONS

1. The action of organic acids on salts

More than twenty years ago Stieglitz (363) pointed out facts which Brönsted's ideas have reëmphasized: many common hydrogen compounds act as weak acids, therefore sodium hydroxide is a salt and the reactions represented by the equations



and



are exactly analogous.

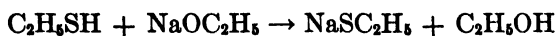
If such reactions are to be employed in preparing salts, a list in which acids are arranged according to strength would be of material service. The extent of displacement, however, varies with temperature and with the effective concentrations of reactants and products. It is necessary, therefore, to specify the former, and to regulate the latter by avoiding the use of solvents in which there is an appreciable divergence in ionization or solubility of reagents and products. After justifying the assumption that salts of weak acids dissolved in diethyl ether are ionized to approximately the same extent, Conant and Wheland (72) established the relative acid strengths of a number of hydrocarbons by such a displacement method. Their results, supplemented by additional information on benzene (124, 430), are abbreviated in table 1, each acid being able to displace those below it more or less completely. It is questionable whether the relative affinities of organic radicals for the electron pair (207), which

TABLE 1
Relative acidity of weak acids

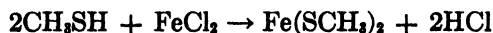
1. Acetophenone	9. 1-Naphthyldiphenylmethane
2. Phenylacetylene	10. Diphenylmethane
3. Indene	11. 1,1-Diphenyl-2-methylethylene (1,1-diphenyl-1-propene)
4. Phenylfluorene	12. Cumene
5. Fluorene	13. Toluene
6. Xanthene	14. Benzene
7. Diphenyl(phenylphenyl)methane	15. Ethane
8. Triphenylmethane	

determine the acidities of their hydrogen compounds, have actually been measured by the relative rates of competitive reactions (6).

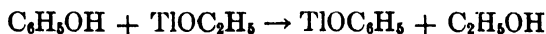
Until the systematic study, as begun by Conant and McEwen (70), of the acidities of amines, alcohols, and mercaptans is farther advanced, judgment must be based on such occasional displacements as have been reported. Sodium sulfide is said to fail to neutralize a mercaptan, and even sodium hydrosulfide produces only a partial reaction (44), so that the ability of cupric sulfide to remove mercaptans from their solutions in hydrocarbons is unusual and unexplained (354). While the soluble alkali metal mercaptides are better prepared by the action of the free acids on metallic hydroxides or alkoxides,



the extreme insolubility of the mercaptides and alkyl selenides of heavier metals makes it possible to precipitate them in the presence of hydrochloric acid.



Although the reaction between an alcohol and a strong alkali like sodium hydroxide is normally far from complete, commercial practice has utilized these cheap materials by continuous dehydration to increase the yield (188, 401, 399). Thallous ethoxide and sodium ethoxide are favored starting materials for preparing other alkoxides by alcoholysis.

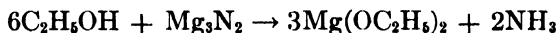


A novel synthesis is that in which a metal otherwise inert toward an alcohol reacts in the presence of oxygen or ozone (241, 199, 121, 84).

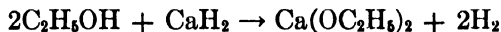


Copper (353, 354) and lead (298) apparently conduct themselves similarly.

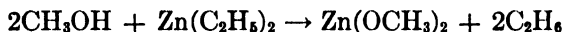
Alkoxides may be secured by the alcoholysis of sodium amide (75, 318, 32, 33, 215), or of the nitride of lithium (108), sodium (405), magnesium (367a, 418), or calcium (275),



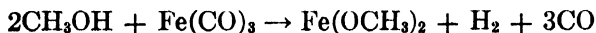
or of calcium hydride (418, 310),



or of a salt of a hydrocarbon (309, 385).



The solvolysis of iron tricarbonyl, a covalent substance, produces impure ferrous methoxide (168),

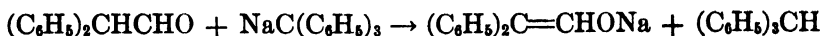


whereas that of ferric formate is more typical in its incompleteness (174).



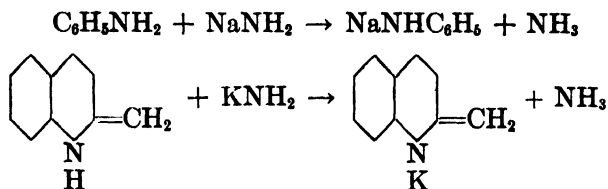
Neither the copper "salt" of acetoacetic ester (420) nor thorium tetraacetyl acetone (38), each a chelate compound, is convertible to a pure alkoxide by an alcohol.

Schlenk, Hilleman, and Rodloff (332) have contributed to our very meager knowledge of salts of aldehyde enols by their study of sodium 2,2-diphenylvinyl oxide, prepared according to the equation

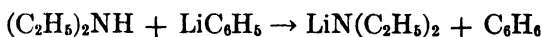


The acidic hydrogen of the $>\text{NH}$ grouping in aromatic amines (384, 271, 414), pyrrole, carbazole, and indole (116), and enolic modifications

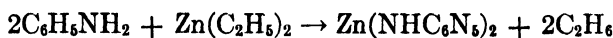
of ammono ketones (31), is replaced by metal when these acids are treated with an alkali amide.



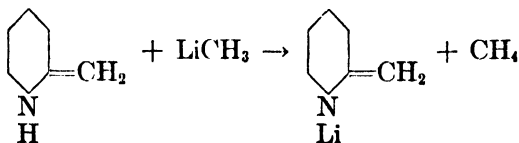
To note some isolated reactions of ammono acids, diethylamine reacts with lithium phenyl (442),



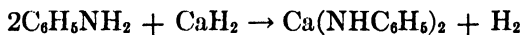
aromatic amines with magnesium diphenyl (329) or zinc dialkyls (115, 126),



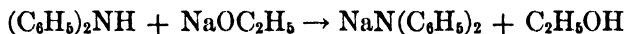
and ammono enols with lithium alkyls (446).



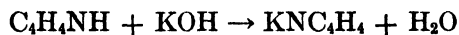
Aromatic amines similarly liberate the weak acid H_2 when they act upon the hydrides of sodium, potassium (90), or calcium (103, 101).



Although most alkyl amides are readily decomposed by water and alcohols, sodium diphenylamide has been partially precipitated from ether (61) as a product of the reaction represented by the equation



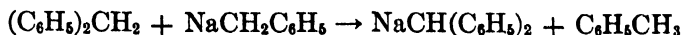
Moreover, fusion methods have succeeded in completing the reaction between potassium hydroxide and pyrrole by volatilizing the water formed (9, 65).



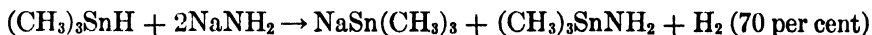
The potassium salts of carbazole (141, 66, 346) and of fluorene (407, 7) have been secured in the same way.

Nevertheless, few metallic derivatives in which the central element belongs to Group IV are accessible by displacement reactions, because of

the weakness of the hydranes as acids. One hydrocarbon sometimes causes the liberation of another (72).

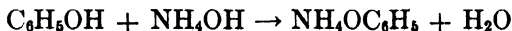


Fluorene (408, 128) and indene (409, 129) react normally when heated with sodium amide or with sodium in the presence of gaseous ammonia. In addition, hydrocarbons containing the benzohydryl group, $(\text{C}_6\text{H}_5)_2\text{CH}-$, are sufficiently acidic in liquid ammonia to decompose potassium amide (434). On the other hand, even the irregularity of the behavior of trimethylstannane (226)



is probably less than that of many other hydranes.

It is perhaps appropriate to refer briefly to ammonium salts of alcohol types, since it may be supposed that they are formed in small amounts by the action of a simple or substituted ammonium hydroxide upon an acid:



Actually the salts so formed can no more be isolated than can ammonium hydroxide itself. Instead, they are secured by the action of an acid on a base (ammonia or an amine) in the Brönsted sense:

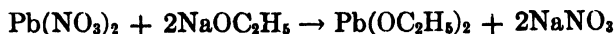


Such reactions have no claim to consideration among acid-salt metatheses, but lack sufficient importance to warrant assigning them to an especially created subdivision.

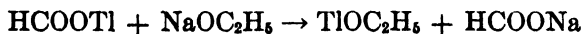
2. Metatheses between two salts

The most widely applicable reaction for preparing salts of alcohol types containing any desired metal, a metathesis between two salts, has never been exploited commensurately with its value. Since formation of a precipitate is a convenient process insuring completion of the reaction, the solvent is chosen with a view toward promoting that effect.

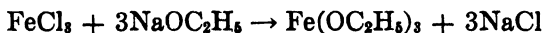
Employment of this double decomposition has been confined mainly to the preparation of alkoxides. Chablay (59) has demonstrated its utility in liquid ammonia, where a reaction like that represented by the equation



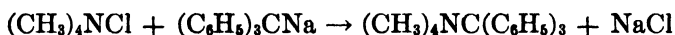
reaches completion by virtue of the small solubility of plumbous ethoxide. Thallous formate, treated with sodium ethoxide in absolute alcohol, yields a precipitate of oily thallous ethoxide (269).



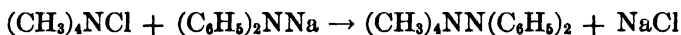
Upon other occasions it is the by-product which is insoluble; sodium chloride is precipitated from alcohol in the synthesis of ferric ethoxide (377),



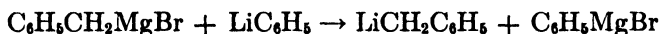
chromic ethoxide (375), lithium ethoxide (197), and others (267). Corresponding metatheses in the methane and the ammonia systems enabled Schlenk and Holtz (333, 334) to obtain some remarkable ammonium salts of hydrocarbons



and amines.



According to Ziegler and Dersh (441), lithium benzyl and some other organolithium compounds are best prepared by the action of lithium phenyl on the corresponding Grignard reagent.



3. *The reaction of salts with other organic compounds*

When alkalis saponify esters, neutralization of the excess alkali by the alcohol may be a secondary change.



A similar conversion occurs during the fusion of aromatic sulfonic acids with sodium hydroxide or sodium amide (34).

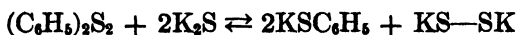


At elevated temperatures, various reagents—fused alkalis (253, 8, 123), aluminum chloride (266), and sodium ethoxide (265)—decompose ethers, sometimes with the initial production of salts of alcohol types; such salts, however, tend to decompose at the temperature required.

In liquid ammonia, sodium amide adds to the free radicals triphenylmethyl (433) and trimethylstannyl (226) in the sense of the equation



Dialkyl disulfides undergo an apparently related reaction,



which is represented as reaching equilibrium, because different authors (295, 178) have reported such exchanges to proceed in opposite directions.

IV. PHYSICAL PROPERTIES

Any exposition of the properties of salts of alcohols and alcohol analogs may well have as its theme the recurring fact that the transition from heteropolar salts to homopolar ortho esters is a stepwise process. This

TABLE 2
Properties of salts of alcohols

SALT	COLOR	FORM	SOLUBILITY			REFERENCES
			ROH	NH ₃	Organic solvents	
LiOC ₂ H ₅	White	C	+	+	(+)	(59, 197, 414, 108)
NaOC ₂ H ₅	White	A	+	—	—	(404, 380, 59, 26, 232)
KOC ₂ H ₅	White	A	+	—	—?	(59, 26, 232)
Cu(OCH ₃) ₂	Blue?	A	—	?	?	(370)
Mg(OCH ₃) ₂	White	C	(+)	?	(+)	(368, 370, 26, 373, 41, 57)
Zn(OCH ₃) ₂	White	A	—	—	—	(385, 26, 267)
Hg(OCH ₃) ₂ ?	Orange	A	—	?	?	(171)
Ca(OC ₂ H ₅) ₂	White	A	+	—	(+)?	(88, 299, 59, 26)
Ba(OC ₂ H ₅) ₂	White	A	+	—	—	(88, 59, 26)
Sr(OC ₂ H ₅) ₂	White	A	+	—	?	(59)
Al(OC ₂ H ₅) ₃	White	C	—	?	(+)	(381, 74, 26, 386, 390)
TiOC ₂ H ₅	White*	C	+	—	+	(241, 59, 121, 84, 64, 269, 351)
Ti(OC ₂ H ₅) ₃	Violet	A	—	?	—	(256)
Zr(OC ₂ H ₅) ₄	White	C	+	?	+	(192, 267)
Pb(OCH ₃) ₂	White	A	—	—	?	(370, 298, 59)
Cr(OC ₂ H ₅) ₃	Green	A	(+)	?	(+)?	(375)
Fe(OCH ₃) ₂	Violet	A	—	?	—	(168)
Fe(OC ₂ H ₅) ₃	Brown	C	(+)	?	(+)	(377)

C = crystalline; A = amorphous. An asterisk denotes that the compound is liquid at ordinary temperatures.

A + sign indicates a considerable solubility.

A (+) sign represents partial solubility.

A — sign indicates practical insolubility.

transition correlates well with that noticeable among metallic halides and oxides. Metals of Groups I and II, with the exception of beryllium and mercury, form salts of alcohol types which are rather involatile and insoluble in most solvents (see tables 2, 3, 4, 5, 6), but predisposed toward ionization if dissolved. Derivatives of all non-metals, antimony, and the tetravalent forms of titanium, germanium, tin, and lead have some or all of the characteristics of organic compounds—definite and relatively low melting points and boiling points, solubility in organic solvents, and

TABLE 3
Properties of salts of mercaptans

SALT	COLOR	FORM	SOLUBILITY		REFERENCES
			Water	Organic solvents	
NaSC_2H_5	White	C	+	(+)	(209, 301)
KSC_2H_5	White	A	+	(+)	(437)
CuSC_2H_5	Yellow	A	—	(+)	(209, 97, 354)
AgSC_2H_5	Yellow	C	—	?	(395, 360, 209)
AuSC_2H_5	White	A	—	(+)	(437, 165)
$\text{Zn}(\text{SC}_2\text{H}_5)_2$	White	C	—	?	(209)
$\text{Cd}(\text{SC}_2\text{H}_5)_2$	White	C	—	?	(209)
$\text{Hg}(\text{SC}_2\text{H}_5)_2$	White	C	—	+	(437, 209)
TiSC_2H_5	Yellow	A	(+)	?	(209)
$\text{Sn}(\text{SC}_2\text{H}_5)_2$	Yellow	A?	—	?	(209)
$\text{Pb}(\text{SC}_2\text{H}_5)_2$	Yellow	C	—	+	(437, 209)
$\text{Bi}(\text{SC}_2\text{H}_5)_3$	Orange	C	—	+	(209)
$\text{Fe}(\text{SC}_2\text{H}_5)_2$	Black	A	—	—	(209, 259)
$\text{Ni}(\text{SC}_2\text{H}_5)_2$	Brown	A	—	—	(209, 261)
$\text{Co}(\text{SC}_2\text{H}_5)_2$	Brown	A	—	(+)?	(209)
$\text{Rh}(\text{SC}_2\text{H}_5)_3$	Yellow	A	—	(+)?	(209, 281)
$\text{Pd}(\text{SC}_2\text{H}_5)_2$	Yellow	A	—	—?	(209, 281)
$\text{Ir}(\text{SC}_2\text{H}_5)_3$	Orange	A	—	(+)	(176, 281)
$\text{Pt}(\text{SC}_2\text{H}_5)_2$	Yellow	A	—	—?	(209, 281, 305)
$\text{Pt}(\text{SC}_2\text{H}_5)_4$	Orange	A	—	—	(176, 281)

See note accompanying table 2.

TABLE 4
Properties of salts of amines

SALT	COLOR	FORM	SOLUBILITY			REFERENCES
			RNH_2	NH_3	Organic solvents	
NaNHC_6H_5	White	A	+	+	(+)	(384, 302, 412, 372, 89, 90)
$\text{NaN}(\text{C}_6\text{H}_5)_2$	White	C	+	+	(+)	(384, 302, 412)
KNHC_2H_5	White	A	+	+	(+)?	(384)
$\text{KN}(\text{C}_6\text{H}_5)_2$	White	A	+	+	(+)	(155, 116)
CaNHCH_3	White	A	+	+	—	(308)
AgNC_6H_5	White	?	?	+	?	(116)
$\text{Mg}(\text{NHC}_6\text{H}_5)_2$	White	A	?	?	—	(372, 329)
$\text{Mg}(\text{NC}_6\text{H}_5)_2$	White	A?	?	(+)	?	(116)
$\text{Zn}(\text{NHC}_6\text{H}_5)_2$	White	A	?	?	—	(115, 126)
$\text{Zn}[\text{N}(\text{C}_6\text{H}_5)_2]_2$	White	A	?	?	—	(115, 126)
$\text{Ca}(\text{NHC}_6\text{H}_5)_2$	White	A	(+)	?	—	(103)
$\text{Ca}[\text{N}(\text{C}_6\text{H}_5)_2]_2$	White	A	(+)	(+)	—	(103)

See note accompanying table 2.

TABLE 5
Properties of salts of hydrocarbons

SALT	COLOR	FORM	SOLUBILITY		REFERENCES
			NH ₃	Organic solvents	
LiC ₂ H ₅	White	C	—	(+)	(426)
LiC(C ₆ H ₅) ₃	Red	C	+	+	(426)
LiCH ₂ C ₆ H ₅	Red	C	(+)?	+	(426)
NaC ₂ H ₅	White	A	—	—	(426)
NaC(C ₆ H ₅) ₃	Red	C	+	+	(426)
NaCH ₂ C ₆ H ₅	Red	C	(+)?	(+)	(426)
KCH ₃	White	A	—	—	(426)
KC(C ₆ H ₅) ₃	Red	C	+	+	(426)
RbC(C ₆ H ₅) ₃	Red	C	+	(+)	(143)
CsC(C ₆ H ₅) ₃	Red	C	+	(+)	(143)
CuC ₆ H ₅	White	A	—?	—	(306)
AgC ₆ H ₅	Brown	A	—?	—	(238, 306)
Mg(C ₆ H ₅) ₂	White	C	(+)?	+	(196)
Cu[C(C ₆ H ₅) ₃] ₂	Red	?	+	(+)?	(223)
Zn(C ₂ H ₅) ₂	White*	C	—	+	(122)

See note accompanying table 2.

TABLE 6
Known properties of ammonium salts of alcohol types

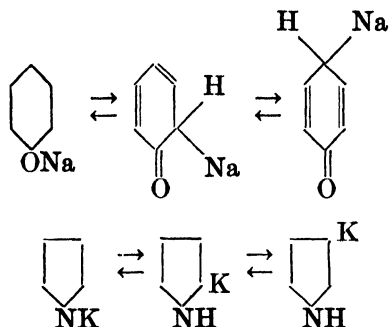
SALT	FORM	SOLUBILITY	REFERENCES
(CH ₃) ₄ NC(C ₆ H ₅) ₃	Red powder	Soluble in pyridine only	(333)
(CH ₃) ₄ NN(C ₆ H ₅) ₂	Green-yellow needles	Soluble in pyridine only	(334)
(CH ₃) ₃ C ₆ H ₅ NOC ₆ H ₅	White fusible powder	Soluble in water	(163)
(CH ₃) ₃ C ₆ H ₅ NSC ₆ H ₅	White fusible powder	Soluble in water	(163)
CH ₃ NH ₂ C(C ₆ H ₅) ₃	Pink solid	Insoluble in liquid NH ₃	(433)
C ₆ H ₅ NH ₂ OC ₆ H ₅	White fusible powder	Soluble in water and organic solvents	(180, 100, 250, 179)
CH ₃ NH ₂ OC ₆ H ₅	White fusible powder	Soluble in methylamine	(132)
NH ₄ C(C ₆ H ₅) ₃	Pink solid	Insoluble in liquid NH ₃	(223)
NH ₄ SC ₆ H ₅	White crystals	Insoluble in liquid NH ₃	(232, 414, 417)

inability to support electrolytic conduction. All other metals, including mercury and beryllium, yield compounds intermediate in nature between salts and esters.

The many similarities between parent substances and alcohol types in each system create expectations that salts of the two should be equally comparable. That such resemblances indeed exist is most clearly seen in the methane system (compare NaCH_3 and NaCH_2CH_3), but sodium hydroxide and a sodium alkoxide also exhibit numerous likenesses.

During the formative period of structural organic chemistry, the constitution of sodium alkoxides was naturally uncertain. Wanklyn considered sodium ethoxide the "hydrate" of a radical called "ethylenesodium," $(\text{C}_2\text{H}_4\text{Na})\text{OH}$, and held that in that salt as well as in sodium alkyls the metal is trivalent (403, 127). The arguments which finally prevailed over this view and which led to the commonly accepted structural formula, $\text{CH}_3\text{CH}_2\text{ONa}$, were the replaceability of only one hydrogen atom per molecule, and the fact that in ethers prepared by the Williamson synthesis the alkyl group introduced is known to be linked through oxygen (243).

It is maintained by Hückel (182), against much opposition, that salts of alcohol types can always exist in tautomeric forms.



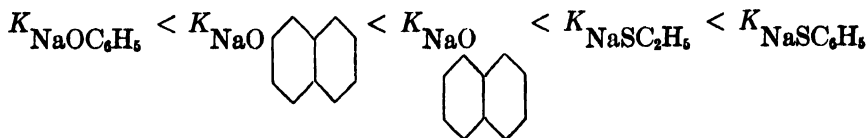
The organometallic isomers are supposed to be present in solution in non-ionizing media, whereas alcohols and other ionizing solvents favor the existence of the orthodox form.

A number of theories have been proposed to account for the color of some metallic salts of triphenylmethane and related acids, but the only one yet extended to apply to all salts of alcohol types is that of Hantzsch. In pursuance of his general theory of pseudo acids, Hantzsch (149, 150) holds that two isomeric forms of a salt of an alcohol type are possible, a covalent and an electrovalent form. The colored salts of triphenylmethane and diphenylamine are electrovalent forms in which the anion contains a quinoid benzene ring. Modern theories of atomic linkages,

however, cast grave doubt upon the possibility of existence of two distinct electroisomers.

Molecular weight determinations have shown sodium ethyl dissolved in zinc diethyl (160), ferric ethoxide in ethyl alcohol (377), and alkali metal salts of simple alcohols dissolved therein (24), to be monomolecular at low concentrations. Sodium and potassium salts of menthol and of the enolic forms of camphor, menthone, and acetophenone dissolved in organic solvents (24), as well as the solvates present in concentrated solutions of alkali alkyls in zinc diethyl (160), exist as at least double molecules, their molecular condition varying with the nature of the solvent. Although older cryoscopic data (381) were interpreted as indicating that aluminum alkoxides in benzene are monomolecular, it is now well-established that both aluminum (390) and thallium (351) alkoxides are considerably associated in that solvent. According to calculations of dipole moments based on their dielectric constants, the polymeric forms of the aluminum salts are symmetrically constituted and probably have a ring structure (390).

A number of investigators have concerned themselves with the heats of formation of alkali metal alkoxides and related salts (83, 84, 85, 27), and with the degree of hydrolysis suffered by alkoxides at various dilutions (139, 379, 283, 46, 406, 56). Bent and Gilfillan (29) have reported that potassium triphenylmethyl behaves as a true salt in a voltaic cell. From conductance measurements made on this and other organoalkali salts dissolved in pyridine, Ziegler and Wollschitt (445) concluded that under these conditions the compounds are highly polar and non-associated. The same relatively high conductances are characteristic of solutions of sodium triphenylmethyl, sodium triphenylgermanyl, and sodium triphenylstannyl in liquid ammonia (213, 222). In this solvent sodium phenylamide is a better electrolyte than sodium amide (213); sodium triphenylmethyl is better than sodium trimethylmethyl; and the dissociation constants of the salts of alcohols and thiols studied (221) assume the order:



A consideration of these facts led Kraus and Johnson (221) to point out that an increase in the size of the anion produces an increase in conductance. A comparison of sodium hydroxide with a sodium alkoxide in this respect has not been made, because no non-reactive solvent for both salts is known. Alcohols have served as solvents in measurements of conduct-

ances (379, 311, 350, 211, 411, 170, 20) and decomposition potentials (55) of alkoxides. Data on refractive indices substantiate the electrical evidence that higher alcohols cannot cause ionization of sodium alkoxides dissolved therein (379, 50).

By way of a summary, it may be concluded that the salt-like character of the salt $M_x(AR_n)_y$ tends to be increased by the following changes:

(a) Increased electropositive nature of M, as indicated by the electrochemical series. Example: sodium phenoxide, $NaOC_6H_5$, is more salt-like than aluminum phenoxide, $Al(OC_6H_5)_3$.

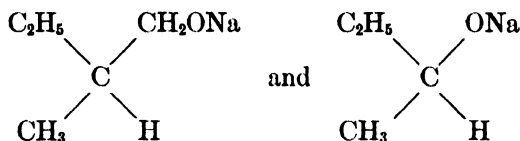
(b) Decreased valence of M. Example: titanium triethoxide, $Ti(OC_2H_5)_3$, is more salt-like than tetraethyl titanate, $Ti(OC_2H_5)_4$.

(c) Increased electronegative nature of A. This may be intrinsic (zinc methoxide, $Zn(OCH_3)_2$, is more salt-like than zinc diethyl, $Zn(CH_2CH_3)_2$), or it may be induced by changes in the kind and number of R groups substituent on the central element.

V. CHEMICAL PROPERTIES

1. *Pyrogenetic reactions*

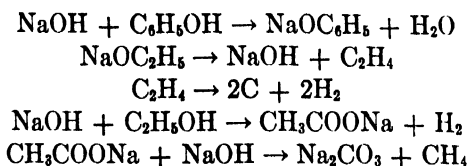
In the case of optically active alkoxides like



decomposition by heat is preceded by racemization. A theory of the mechanism of such transformations, proposed by Hückel and Naab (183, 181) and accepted in subsequent work (362), holds that steric rearrangements of alkoxides always occur at the asymmetric carbon atom or one immediately adjacent thereto, and that they proceed through intermediate formation of a salt of an enolic form.

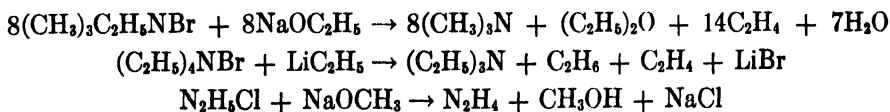
Not many other salts of alcohol types have been so carefully studied as regards pyrolytic reactions, although all are subject to thermal decomposition; indeed, silver phenyl (238, 306) and many salts of enolic forms of aldehydes and ketones, e.g., sodium vinyl oxide (118), $CH_2=CHONa$, are unstable even at ordinary temperatures. Judging from the work of Norris (289), it is of prime importance to control all variables (time, temperature, and pressure), if data on the kinds and amounts of products are to have any significance. In the simple destructive distillations which are our chief source of information, such control has usually been neglected. These studies are further complicated by numerous simultaneous and

consecutive side reactions, as Nef (284) and Fry and coworkers (123) have shown.

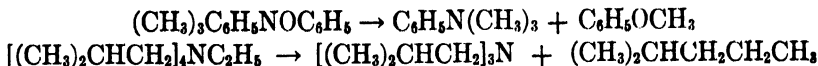


Differences in the nature of alkyl groups present vary the course of the reaction in each system; sodium methoxide, sodium ethoxide, and sodium phenoxide yield compounds dissimilar in quality and quantity. (See table 7.) When it is added that decomposition products of corresponding salts of different metals are often widely divergent in character, the absence of inclusive rules is accountable. Two minor uses of pyrolytic reactions involving aluminum salts are noteworthy. The destructive distillation of aluminum aryl oxides produces good yields of aromatic ethers (138, 382, 74, 273), while similar treatment of the aliphyl oxides leaves a residue of activated aluminum oxide particularly valuable as a dehydration catalyst (5).

Presumably tetraalkylammonium aliphyl oxides (274, 272, 397, 1, 189), tetraalkylammonium (146) and tetraalkylarsonium (121a) salts of alkanes, and hydrazinium methoxide (82) can exist only at low temperatures. The reactions which should give rise to them at higher ones yield only decomposition products.



The implied pyrolysis of the intermediate salts follows the same course as that taken by more stable derivatives of this kind (163, 157, 167).



2. Metathetic reactions

Mention has already been made of the fact that metallic derivatives of alcohol types may be secured by a metathesis between two salts, one of which is often a halide:

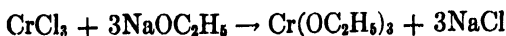
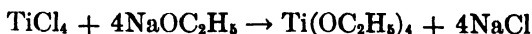


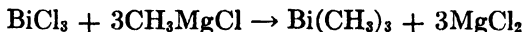
TABLE 7
Pyrolysis of salts of alcohol types

SALT	TEMPERATURE	MAIN PRODUCTS REPORTED	REFERENCES
	<i>degrees C.</i>		
NaOCH_3	260-400	Na_2CO_3 , Na_2C_2 , C, H_2 , CH_4	(23, 98)
NaOC_2H_5	250-350	NaOH , Na_2CO_3 , CH_3COONa , Na_2C_2 ?, C, H_2 , CH_4 , C_2H_4	(404, 270, 284, 73, 98)
NaOC_6H_5	450-500	NaOH , C, CH_4 , C_2H_6 , C_6H_6 , (C_6H_5) ₂	(98, 110, 175, 173)
$\text{NaOCH}(\text{CH}_3)_2$	200	NaOH , $\text{CH}_3\text{CH}=\text{CH}_2$	(40)
$\text{Mg}(\text{OCH}_3)_2$	80	MgO , H_2 , CO, CH_4	(368)
$\text{Zn}[\text{OCH}_2\text{CH}(\text{CH}_3)_2]_2$?	$[\text{ZnO}]?$, H_2 , CO, CO_2 , $\text{C}_n\text{H}_{2n+2}$, C_nH_{2n} , ROH, RCHO, RCOOR	(385)
$\text{Ca}(\text{OC}_2\text{H}_5)_2$?	CaCO_3 , (CH_3) ₂ CO, H_2 , CH_4	(88)
$\text{Ca}(\text{OC}_6\text{H}_5)_2$?	$[\text{CaO}]?$, $\begin{array}{c} \text{C}_6\text{H}_4 \\ \diagup \quad \diagdown \\ \text{O} \end{array}$, C_6H_6 , H_2O	(396)
$\text{Ba}(\text{OC}_2\text{H}_5)_2$?	BaCO_3 , C, H_2 , C_2H_4 , CH_4 , C_2H_6 , C_4H_{10}	(239a, 64, 88)
$\text{Al}(\text{OC}_6\text{H}_5)_3$	265	Al_2O_3 , (C_6H_5) ₂ O	(138, 382, 74, 273)
TlOC_2H_5	?	Tl, $\text{C}_2\text{H}_5\text{OH}$, CH_3COOH , H_2	(241)
$\text{Pb}(\text{OC}_6\text{H}_5)_2$?	$[\text{Pb}]?$, $\begin{array}{c} \text{C}_6\text{H}_4 \\ \diagup \quad \diagdown \\ \text{O} \end{array}$, H_2O	(140, 25)
NaSCH_3	200	Na_2S , Na_2S_2 , [(CH_3) ₂ S]?	(437, 209, 301)
Mercaptides of Au, Hg, Pt..	Various	Metal, dialkyl disulfide	(95, 209, 294, 165)
Other mercaptides.....	Various	Metallic sulfide, dialkyl sulfide	(202, 360, 95, 209)
AgSeC_6H_5	?	Ag, (C_6H_5) ₂ Se ₂	(93)
KNHC_2H_5	300?	KCN, C, H_2	(384)
KNHC_6H_5	?	KCN, C	(172)
$\text{KNC}_{12}\text{H}_5$	400?	KCN, C, NH_3 , $\text{C}_{12}\text{H}_5\text{NH}$	(62)
CsNHCH_3	120	CsCN , H_2	(308)
CsNHC_2H_5	110	$[\text{CsCN}]?$, H_2 , $\text{C}_n\text{H}_{2n+2}$, C_nH_{2n}	(308)
NaCH_3	200	Na_2C_2 , Na, CH_4	(37, 54)
NaC_2H_5	100	NaH , C_2H_4 , C_2H_6 , [Na_2C_2]?	(37, 54)
LiC_2H_5	120	LiH (50 per cent)	(378)
LiC_2H_5	250	Unsaturated hydrocarbons, C_2H_6 , H_2	(121a)
LiC_4H_9	173	Butylene, butane, H_2	(121a)
CuC_6H_5	80	Cu, (C_6H_5) ₂	(306)
AgC_6H_5	-18	Ag, (C_6H_5) ₂	(238, 306)
$\text{Mg}(\text{C}_6\text{H}_5)_2$	175	MgH_2 , C_2H_4	(196)
$\text{NaSn}(\text{CH}_3)_3$	75	Na-Sn alloy, [$\text{Sn}(\text{CH}_3)_4$]?, hydrocarbons	(229)

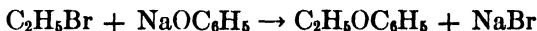
When the reacting halide is highly covalent, one product is an ortho ester of an inorganic acid.



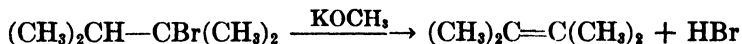
It may be recalled that the Grignard reagent is favored as a means for preparing organometallic derivatives by this method.



The similarity of all these reactions to that represented by the equation

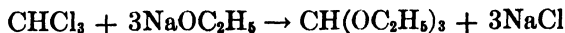


is so marked that we may regard them as modifications of the original Williamson synthesis. This synthesis, in which alkoxides play a part similar to that of metallic hydroxides in saponification, is subject to all the limitations that might be anticipated from this analogy. Aryl halides readily surrender their halogen only when a copper catalyst is present (391). Again, a hydrogen atom may combine with one of halogen bound to an adjacent carbon atom, producing unsaturation:

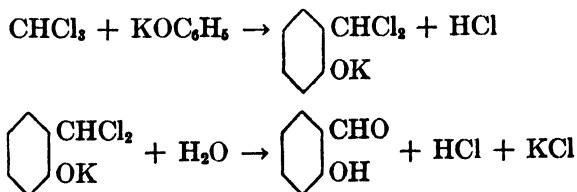


Britton (49) reported that temperature considerably influences the course of the reaction between sodium phenylamide and phenyl chloride; at 180°C. the chief product is diphenylamine, whereas at 250°C. *o*-aminobiphenyl is obtained in 45 per cent yield.

The behavior of polyhalogenated hydrocarbons is difficult of prediction. Sodium ethoxide couples normally with chloropicrin (152) and chloroform (201),

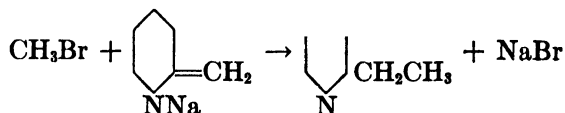
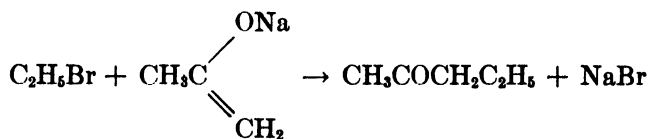


but aryl oxides and mercaptides may either give the expected ortho esters (125, 16) or undergo ring substitution or oxidation, depending on experimental conditions (35, 285, 257, 25, 216). The Tiemann-Reimer reaction is one of these abnormal cases:



Chloroform and carbon tetrachloride react similarly with potassium pyrrole, yielding α -pyrrolealdehyde (19) and α -pyrrolecarboxylic acid (67),

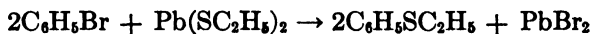
respectively. When employed in a Williamson synthesis, salts of enols may yield, instead of the expected ether-like compounds, the isomeric alkylated keto forms (33).



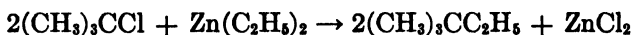
It is Hückel's (182) contention that most of these and other so-called "abnormal" Williamson reactions are normal couplings involving the organometallic forms of salts of alcohol types.

Under proper control, nevertheless, the Williamson reaction attains quantitative precision in the Stephanow method for determination of covalent halogen (361, 320). Its freedom from side reactions and the possibility of varying the degree of ionization of the reacting salt by changing the solvent make this coupling eminently suitable for studies in reaction kinetics.

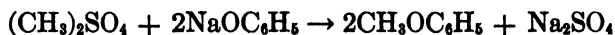
Just as sodium ethoxide, in the Williamson synthesis, is employed to supply an $-\text{OC}_2\text{H}_5$ group, salts in other systems (sodium mercaptides, lead mercaptides, sodium diaryl amides, etc.) are used to introduce the negative groups they contain.



Zinc dialkyls have been superseded by Grignard reagents in most fields, but they are still superior to their competitors for preparing pure hydrocarbons from tertiary alkyl halides (286).

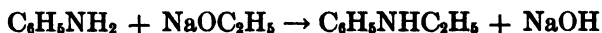


Closely allied to the Williamson synthesis are other reactions in which the rôle of the halogen is played by some other negative group:

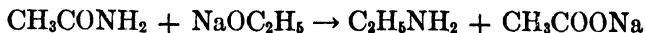


It is well authenticated, however, that esters of fatty acids are not saponified by alcoholic solutions of alkoxides unless water is present to liberate metallic hydroxides (291, 52, 145, 355, 349, 4, 191).

More difficulty is encountered in classifying a high-temperature process which affords a means for replacing many hydrogen atoms by alkyl groups,

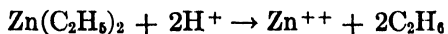


since it is evidently not a true variation of the Williamson reaction. Nitrogen compounds are especially susceptible to such alkylation, which has proved successful for pyrroles (109), pyrazolones (425), and amines (284, 244). If an acyl group is present, as in acetamide or acetanilide, the metallic hydroxide formed effects its removal (345).



In some instances, particularly when alcohols (284, 144, 410, 181) are alkylated, the side reactions produced by sodium alkoxides are so dominant that it is necessary to substitute salts of aluminum or magnesium.

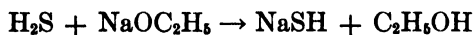
Metatheses between acids and salts find numerous minor uses. Because alkoxides of alkali metals and aluminum, when dissolved in organic liquids, tend to produce a precipitate of metallic hydroxide by reaction with water, they have been of service in determining the dryness of ether (314), alcohols (162), and pyridine (104). Sulfur compounds in benzene are detected by their conversion of soluble thallous ethoxide into insoluble thallous sulfide (269). Again, zinc diethyl dissolved in pyridine comports itself like a Grignard reagent in testing for active hydrogen atoms (154).



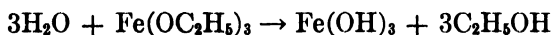
In some cases salts of alcohol types are involved in withdrawing undesirable acids from solution. Mercaptans are removed, in the "sweetening" of petroleum, as their lead salts. The drying of an alcohol by means of the corresponding alkoxide of sodium (79, 356), calcium (242, 310), magnesium (41, 254), or aluminum (105, 153, 400) depends upon regeneration of the alcohol by hydrolysis of the salt. Whether a particular alkoxide is suitable for the purpose depends on its oxidizability and solubility relationships; it is desirable that the solubility of the alkoxide shall be high and that of the hydroxide low (79, 51, 290). Less frequently alkoxides are used to abstract water (203, 386) or hydrochloric acid (204, 386) formed in the course of a reaction. The splitting out of hydrogen halide from adjacent carbon atoms is catalyzed as well as forced to completion by these alkalies.

In other instances the acid or the salt produced by metathesis is desired. The former is the case when salts of alcohol types, made as purification intermediates, are hydrolyzed to yield mercaptans, pyrroles (65), carbazole (141), or the more acidic hydrocarbons like fluorene (408, 7, 128) and indene (409, 129). Salts of alcohols (especially of phenols) are sometimes preferred to the free acids as antiseptics and disinfectants, because of the higher solubility and lower toxicity of the salts. Sodium derivatives of weak organic acids like phthalimide (148), acetoacetic ester, acid amides (42, 119), and higher alcohols (388, 321, 316), are conveniently secured by

neutralizing these acids with sodium ethoxide or sodium methoxide. Even sodium alkyls are reported valuable for preparing salts of alkylated acetonitriles (186), and aluminum alkoxides for manufacturing aluminum carboxylates (187). Exceptionally pure salts of inorganic acids are similarly accessible; hydrogen sulfide (317, 197, 312) and hydrogen selenide (387, 21) form hydrosulfides and hydroselenides of alkali metals,



and electrolyte-free colloidal hydroxides of iron and chromium are produced by hydrolysis of the metallic ethoxides (375, 376, 377).



3. Oxidation-reduction reactions

To avoid occasion for misapprehension it should be explained that a few oxidations of salts of alcohol types are later discussed as addition reactions. Such a process as the addition of sodium alkyls to molecular oxygen is incidentally an oxidation, but it corresponds more closely to the addition of sodium alkoxides to carbon dioxide.

If these conversions are excluded, the primary products of oxidation are a new metallic salt and a coupled pair of organic residues:



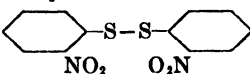

If $\text{R}_n\text{A}-$ is capable of existing as a free radical, further oxidation is likely to produce a peroxide, $\text{R}_n\text{A}-\text{O}-\text{O}-\text{AR}_n$. The oxygen representative $\text{RO}-\text{OR}$ is usually too unstable to persist, and consequently there result aldehydes, carboxylic acids, and more complex degradation fragments. A very active oxidant, e.g., a halogen, may enter the disintegration residues as a substituent.

Instances in which salts of metals other than sodium or potassium have been oxidized to recognizable products are rare; a notable exception is the preparation of aliphatic sulfonic acids by boiling lead mercaptides with nitric acid (287). Of the reductions tabulated in table 8, the only ones of consequence are those accomplished by alkoxides. Since reducing power seems to vary inversely as extent of ionization, alkoxides of high molecular weight far surpass aryl oxides in this respect, while alkoxides of low molecular weight are of intermediate potency. In practice, ionization is minimized by maintaining the concentration of the solution at a high level and adding benzene or some similar non-ionizing medium (366). The work of Diels and Rhodius (92), in which they achieved reduction, by sodium amyloxide, of diverse unsaturated molecules (see table 8), has been adversely criticized by Toussaint (386), but is otherwise generally

TABLE 8
Reductions by salts of alcohol types

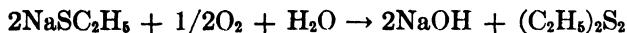
REDUCING AGENT	OXIDIZING AGENT	MAIN PRODUCTS REPORTED	REFERENCES
NaOR.....	O ₂	RCOONa, H ₂ O, Na ₂ O ₂	(161, 284, 48, 14, 169)
	Cl ₂	RCl, RCHO, RCOOH, substituted derivatives, NaCl	(258, 323, 73)
	Br ₂	ROH, RBr, RCOOH, substituted derivatives, NaBr, RCOONa	(258, 348, 22)
	I ₂	Polyiodo hydrocarbons, ROH, HCOOR, NaI, RCOONa	(53, 258, 206, 278, 47, 184)
	CrO ₃ , MnO ₂	RCHO, RCOOH	(73)
	S ₂ O ₃	Na ₂ SO ₃ , Na ₂ S ₂ O ₃ , Na ₂ S ₂ O ₆ , etc.	(394, 424)
	HNO ₃	RNO ₂ , CO ₂	(73)
	NO	N ₂ O, RCHO	(415, 416)
	C ₆ H ₅ N ₃	C ₆ H ₅ NH ₂ , <i>N</i> -phenyl triazole, N ₂ , NaOH	(36, 37)
	Aromatic nitro compounds	Azoxy, azo, hydrazo or amino compounds, Na ₂ C ₂ O ₄	(366, 255, 80, 112)
	Aromatic azo compounds	Hydrazo compounds, alkylated amines	(92)
	C ₆ H ₅ N=CHC ₆ H ₅	C ₆ H ₅ NHCH ₂ C ₆ H ₅	(92)
	C ₆ H ₅ CH=CHCOOH	C ₆ H ₅ CH ₂ CH ₂ COOH	(92)
KOR.....	Aromatic nitroso compounds	Azoxy compounds	(344, 151)
	C ₆ H ₅ NHOH	C ₆ H ₅ N=NC ₆ H ₅ , O C ₆ H ₅ N=NC ₆ H ₅	(17, 18)
NaSR.....	O ₂	R ₂ S ₂ , NaOH	(209, 39)
	I ₂	R ₂ S ₂ , NaI	(257)
	S	R ₂ S ₂ , Na ₂ S ₂	(39)
	Na ₂ S ₂	R ₂ S ₂ , Na ₂ S	(39)
	K ₂ S ₂ O ₈	R ₂ S ₂ , K ₂ SO ₄ , Na ₂ SO ₄	(94)
	SOCl ₂ , SO ₂ Cl ₂	R ₂ S ₂ , SO ₂ , NaCl	(77)
	R'SSO ₂ R'	RSSR', R'SO ₂ Na	(113)
	(R'SO ₂) ₂ S	R ₂ S ₂ , R'SO ₂ Na, R'SO ₂ SNa	(113)
	R'SSO ₂ Na	RSSR', Na ₂ SO ₃	(113)
	Na ₂ S ₂ O ₆	R ₂ S ₂ , Na ₂ SO ₃ , Na ₂ S ₂ O ₃	(113)
	Na ₂ S ₂ O ₄	R ₂ S ₂ , Na ₂ S ₂ O ₃	(113)
	C ₆ H ₅ ICl ₂	R ₂ S ₂ , C ₆ H ₅ I, NaCl	(436)
	C ₆ H ₅ NO ₂	R ₂ S ₂ , C ₆ H ₅ NH ₂	(209)
	CBr ₄ NO ₂	R ₂ S ₂ , CO ₂ , N ₂ , CO, NO, N ₂ O ₂ , NaBr	(239)
	CCl ₄	R ₂ S ₂ , CH(SR) ₂	(13)

TABLE 8—*Concluded*

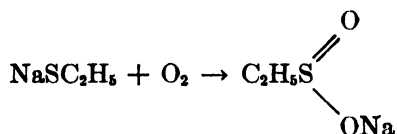
REDUCING AGENT	OXIDIZING AGENT	MAIN PRODUCTS REPORTED	REFERENCES
KSR.....	K_2S_2	R_2S_2, K_2S	(178)
	NH_2OH	R_2S_2, NH_3, KOH	(106)
		 SK	(249)
	CCl_3NO_2	R_2S_2, CO_2, N_2, KCl	(285)
NaNHR...	O_2	$RN=NR, NaOH$	(384, 10)
	$C_6H_5NO_2$	$C_6H_5N=NC_6H_5$, phenazine	(423)
NaNR ₂	I_2	R_2N-NR_2, NaI	(61)
KNHR.....	O_2	$RN=NR, [KOH]$	(10)
KNR ₂	$(C_6H_5)_2S_2$	$R_2NSC_6H_5, KSC_6H_5$	(341)
NaR	O_2	ROOR or R—R, Na_2O_2	(335, 228, 428)
	$(C_6H_5)_2S_2$	$RSC_6H_5, NaSC_6H_5$	(341)
	$(C_6H_5)_2Se_2$	$RSeC_6H_5, NaSeC_6H_5$	(341)

accepted as valid. Aldehydes present seem to influence the rate of reduction of aromatic nitro compounds by potassium ethoxide in a manner yet unexplained (15).

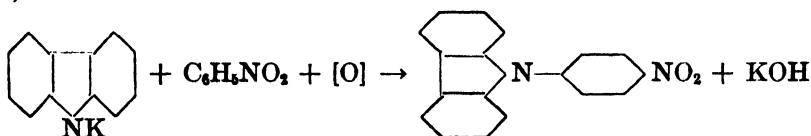
One of the most instructive oxidations of a salt not referable to the water system was studied by Klason (209). Sodium ethyl sulfide in solution is oxidized to diethyl disulfide,



but when dry it merely adds to molecular oxygen, forming sodium ethyl sulfinate.



An extremely peculiar combination of oxidation and alkylation occurs when the potassium salt of carbazole is heated with excess nitrobenzene (86).

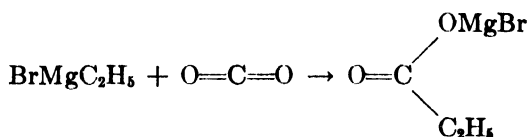


The additional nitrobenzene seems to supply the necessary oxygen, but no mechanism for the reaction has been suggested.

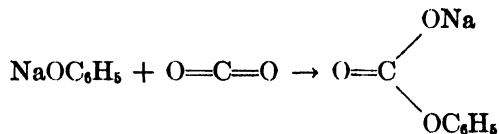
Compounds of disputed structure are formed when nitric acid acts on mercaptides of divalent iron, nickel, or cobalt. Manchot (260) defends the belief that $\text{Fe}(\text{NO})_2\text{SR}$, for example, is a covalent derivative of monovalent iron, while Reihlen (307) prefers a polymeric formula requiring main valence linkages through nitrogen and oxygen.

4. Additive reactions

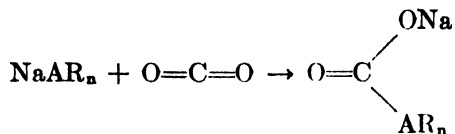
The previously noted addition of dry sodium mercaptide to oxygen is closely allied to reactions useful for the synthesis of carboxylic acids by the Grignard method,



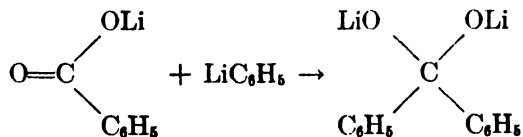
the Kolbe process,



and, in general, by the reaction



Grignard reagents and lithium aryls (134) sometimes add to the second double bond in carbon dioxide,



ketones being formed upon hydrolysis of the reaction product. The tendency of molecules of salts of alcohol types to add to carbon dioxide and other molecules containing multiple bonds may be judged from table 9.

TABLE 9
Addition of salts to unsaturated molecules

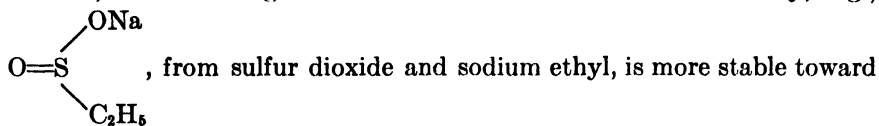
MOLECULE	SALT					
	MR	RMgX	ZnR ₂	M(NHR) _n	M(OR) _n	M(SR) _n
R ₂ C=CR ₂ ...	(+) (431)	— (328)	—	—	—	—
S.....	+ ?	+ (328)	?	?	—	(+) (96)
R ₂ CO.....	+ (426)	+ (328)	— (135)	+ (49)	(+) (393)	—?
RCOOR.....	+	+ (328)	— (135)	?	(+) (393, 99, 3, 325, 357)	?
CO.....	+ (426)	(+)(111)	— ?	?	(+) (23, 359, 326)	?
O ₃	+ (443)	+ (328)	— (122)	—	—	(+) (209)
CO ₂	+ (136)	+ (328)	— (122)	(155, 103, 372)	(368, 382, 107)	— (177, 397, 210)
CS ₂	+ (341)	+ (328)	— (122)	+ (103)	+	+ (280, 177)
SO ₂	+ (426)	+ (328)	+ (122)	+ (103)	(324, 368, 315, 382)	+?

A + sign indicates ready reaction.

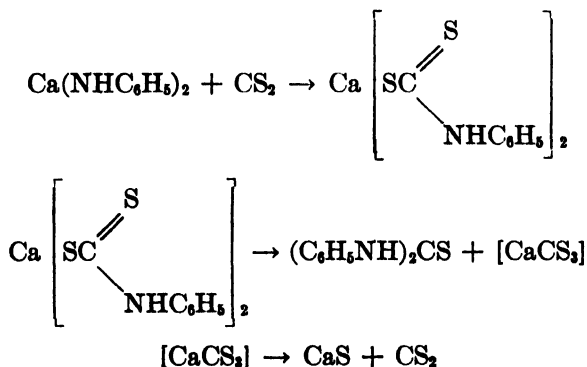
A (+) sign represents infrequent or difficult reaction.

A — sign denotes absence of reaction.

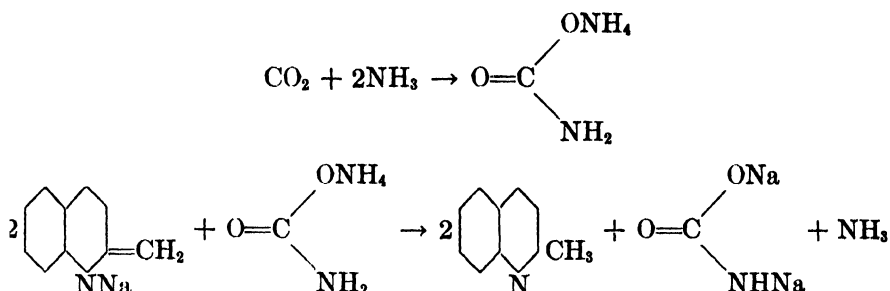
When Grignard reagents or other salts of hydrocarbons add in this manner, the resulting substances exhibit diminished reactivity, e.g.,



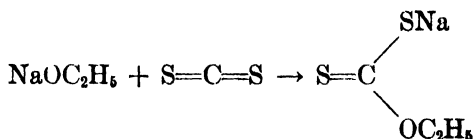
heat and chemical reagents than sodium ethyl itself. Any similar product derived from a salt of another system, however, tends to be decomposed by water or increased temperature with regeneration of part or all of the unsaturated reagent (103, 107).



It may be hazarded that the anomalous failure of salts of enolic (enamic) forms of ammono ketones to add to carbon dioxide in liquid ammonia (31) is due to their considerable tendency to revert to the orthodox structure in the presence of even weak acids.

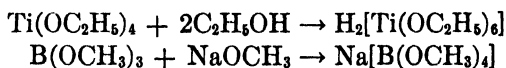


The addition of alkoxides to carbon disulfide produces the xanthates,



of commercial importance in fumigation and ore flotation processes.

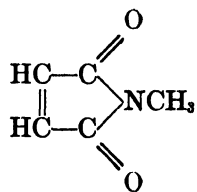
Like many inorganic ortho acids of the water system, the derived ortho esters combine with many donor molecules (267, 327).



Meerwein and Bersin (267) have proved that these alkoxo acids and salts surpass their hydroxyl analogs in stability, presumably because the co-ordinated groups can not easily split out molecules of an ether. The alkoxo acids, although less stable, may occasionally be isolated (377). Many of the so-called salts can even be dissolved in organic solvents and distilled, so that their polar nature must be feeble. The unusual stability and fusibility of the double compounds of alkali alkyls and zinc dialkyls (402, 143), together with their electrical behavior (156, 158, 159, 160), indicate that they belong to this group; consequently $\text{NaC}_2\text{H}_5 \cdot \text{Zn}(\text{C}_2\text{H}_5)_2$ is to be written as $\text{Na}[\text{Zn}(\text{C}_2\text{H}_5)_3]$. Nevertheless, salts of the type $\text{M}[\text{BR}_4]$ can not be secured by the reaction of boron trimethyl or boron triphenyl with an alkali metal alkyl (378).

The uncertainty concerning the structure of the brightly colored addition compounds between polynitro aromatic hydrocarbons and alkali alkoxides does not seriously detract from their merit for identifying the

nitrated derivatives (190, 319, 392). Potassium aryl sulfides similarly add to chloropicrin (285), and unsaturated imides like



yield colored compounds with sodium alkoxides (303).

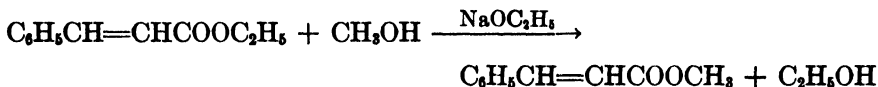
The metals of salts of alcohol types may themselves operate as co-ordination centers for many donor molecules, including those of alcohols, ethers, ketones, and esters. True alcoholates and etherates so obtained ($\text{NaOC}_2\text{H}_5 \cdot 2\text{C}_2\text{H}_5\text{OH}$ or $\text{CH}_3\text{MgBr} \cdot (\text{C}_2\text{H}_5)_2\text{O}$) differ little from the unsolvated salts in chemical properties, but may offer considerable resistance to removal of the solvent.

5. Catalytic effects

This field, a large one in itself, is thoroughly reviewed in Houben's reference work (264, 166, 203), and most of its practical aspects are discussed by Toussaint (386). The treatment here will therefore be confined to lending occasional supplementary emphasis.

Many of the studies in reaction kinetics which led Acree (263, 371, 279) to favor the "dual theory" of catalysis were concerned with alkali alkoxides. Whatever the mechanism may be, the effect of catalysis by alkoxides is evident in various migrations of multiple bonds, tautomeric shifts, and racemizations, the extent of the latter being a basis for quantitative determinations of salts of alcohols (389).

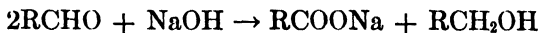
Alcoholyses in which esters exchange alkyl groups with alcohols



require little additional description. Alkoxides of sodium, potassium, and aluminum are the usual catalysts, although Verley (393) and Terentiev (374) have employed the magnesium salts.

The aldol condensation is ordinarily induced by compounds other than sodium ethoxide, but the latter has received much notice in connection with the preparation of acetoacetic ester. Ethoxides of lithium (313) and calcium (299) lack the marked ability of the sodium salt to catalyze this famous reaction, the mechanism of which remains a subject of controversy.

Of much more industrial significance, especially in the manufacture of organic solvents, is a change which may be termed the generalized Cannizzaro reaction. It embraces all oxidation-reduction processes in which only the carbon atom of a carbonyl group and that of any organic molecule are the two active participants. The original Cannizzaro reaction, catalyzed by strong alkalis, may be represented by the equation



Subsequently Claisen (68) discovered that, if sodium alkoxides are employed as alkalis, the intermediate ester is not saponified:

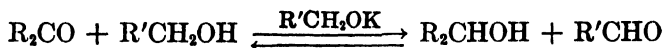


In 1906 Tschtschenko (383) reported an improvement in the yields of ester when the less caustic aluminum alkoxides are substituted for the alkaline catalysts. More recently published researches and patents (288, 292, 102, 200, 282, 81, 386) indicate that a "crossed" reaction between two different aldehydes is equally practical.



Much interest has naturally centered about the relative catalytic values of salts of different metals, and the use of even zirconium alkoxides has been patented (185, 267a). Sodium alkoxides, as might be supposed, usually favor too many side reactions, particularly aldol condensations and resinification (393, 268). While symmetrical diacid alkoxides like $\text{Mg}(\text{OR})_2$ are inferior in effectiveness to the mixed type XMgOR (142), it is the consensus of opinion that activated aluminum compounds excel (63, 102, 268, 304, 91, 198).

Examples of an additional variation of the generalized Cannizzaro reaction were first reported by Montagne and other investigators (252, 435, 358, 147, 284, 276) as ordinary reductions by means of alcoholic potash.



As Ponndorf (304) and Hückel and Naab (183) have pointed out, this modification always involves a reversible exchange of oxidation stages between the central carbon atom of a primary or secondary alcohol and that of a carbonyl group. The velocity of the reaction naturally varies with the reactivity of these two atoms and the efficacy of the catalyst. Verley (393), Dworzak (99), and others have proposed mechanisms based on addition compounds as intermediates, but no agreement has been reached. Although Bachmann (11) has obtained good yields using a

sodium alkoxide as catalyst, the aluminum salts are generally preferred in spite of the increased seriousness of the Tischtschenko ester coupling as a side reaction (268, 322).

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SIGNIFICANT STUDIES IN THE ORGANIC CHEMISTRY OF SULFUR

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It is proposed in this article to indicate how some of the results recently reached in investigating sulfur compounds have important repercussions on general chemical theory. It is not so much an exhaustive review of sulfur work as an attempt to indicate how chemistry as a whole might benefit by a more general knowledge of the results of those who concern themselves specially with sulfur. A very instructive example of the need for this will be found in some recent work on orientation in the benzene nucleus (124).

The line of treatment has permitted the exclusion of certain topics such as the sulfite wood pulp process (1, 2, 3, 3a), the commercial aspects of mercaptans (4), the nature of sulfur dyes (5, 6, 7), and the stereochemistry of sulfoxides (8, 58), all of which have, for other reasons, recently been much to the fore. Of the elements commonly occurring in organic compounds, sulfur can exhibit the greatest variety of valency forms in comparatively stable compounds. This is one reason for the diversity of problems on which some light may be thrown by the behavior of an appropriate sulfur derivative. No attempt has been made to fuse this paper into a continuous narrative, for it is felt that that would only serve to create the false impression that many of the topics had been satisfactorily correlated with the main body of chemical theory; whereas their real significance is that they are very imperfectly explained inclusions in the alloy which modern research is producing.

The aldehyde bisulfite compounds are probably the most generally familiar of the subjects discussed. The sum of evidence here compels us to exclude all ordinary chemical formulas, and it may well be that one of the new types of formulation suggested will find wider application.

Nine years ago glutathione had been isolated and "synthesized." Today its constitution is far from decided, and it seems that the purer it is obtained, the less does it behave in vitro as its biological significance would make us expect.

The direction of addition of unsymmetrical addenda to ethylenic link-

ages has been viewed from numerous angles and speculations have been as numerous. In sharp contrast to all these theories is the valuable work of Kharasch (9), marking peroxide impurity as a major source of confusion and incidentally substantiating the highly significant but rather inadequate experiments of Posner (10) on the addition of mercaptans to unsaturated compounds.

Many lines of work have combined to demonstrate that the coordination bond is as real as an electrovalent or covalent bond. One of the most convincing of these is to be found in Mann's resolution of β,β -diaminodiethyl sulfide platinichloride (12). Mann has also to his credit the resolution of a sulfamide complex which has the distinction of being the second compound containing no carbon whatever to be resolved. In developing his idea of covalency maxima Sidgwick stressed the fact that it was in their compounds with fluorine that elements were most likely to attain this maximum. It seems probable that this may be the underlying reason why sulfonyl fluorides behave quite differently from sulfonyl chlorides with Grignard reagents (11).

The very close similarity between thiophene and benzene prompted Hinsberg (13) to adopt a model of the sulfur atom in which the valencies of sulfur proceeded from *two* centers. The five-membered thiophene was in his view virtually a hexagon. His idea never gained much acceptance, and, with the advent of the Bohr atom, it was abandoned. (Nevertheless, it served its purpose in attracting attention to several cases of isomerism which have received quite interesting explanations.) Still there is no escaping the extraordinary parallelisms between benzene and thiophene, and Erlenmeyer and Leo (14) are to be complimented on introducing fresh life into the old problem by regarding one $-\text{CH}=\text{CH}-$ as pseudo sulfur, and hence benzene as a pseudo pentagon.

Methylene groups can be activated by adjacent SO_2 as well as by CO , but the former present simpler conditions, as the work of Shriner (17) and of Arndt (18) shows that nothing parallel to keto-enol tautomerism takes place. Sulfonylmethanes are weakly acidic; trisulfonylmethanes comparable with chloroacetic acid. Attempts to realize an optically active *ion* of this type were unsuccessful (19), and the problem remains unsolved, although Kipping (20) has succeeded in resolving a compound in which the central $\text{C}-\text{H}$ linkage is not an electrovalency.

The question of transmission of the effects of an atom through space, rather than along the intervening chain of atoms, is being exhaustively studied by Bennett (21). Frequent reference is made to inter- and intramolecular rearrangements which, so far as our present knowledge goes, are peculiar to sulfur chemistry, though they are probably only special cases of more general types.

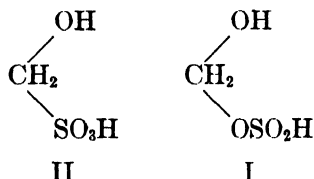
The thioketones developed by Schönberg's school demonstrate remarkable similarities to the compounds of trivalent carbon, and probably represent the high water mark of technique in this field, culminating in the recent demonstration of the monovalency of sulfur (22).

The writer hopes that in the following pages sufficient detail of these important advances is given so that it will be evident how little is definitely settled—how much remains to be done.

FORMALDEHYDE BISULFITE

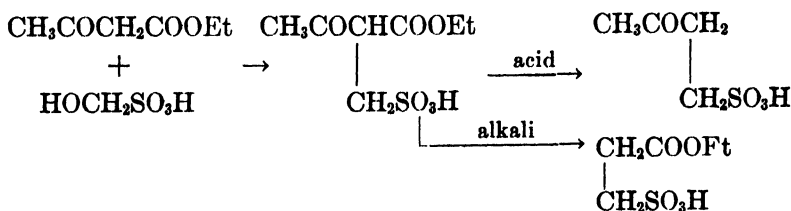
The formula of the formaldehyde bisulfite compound has been attracting fresh interest. Naturally, it includes by implication the bisulfite compounds of all aldehydes (23, 23a).

Of the alternatives which have been seriously considered formula I has, until recently, been preferred to II,



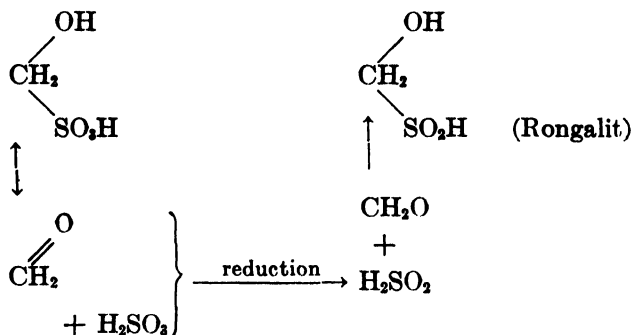
as formula II was claimed for the product obtained by sulfurating methyl alcohol (23b). Moreover, sulfonic acids are in general resistant to reduction, so that the well-known formation of sodium formaldehydesulfoxylate (Rongalit) by reduction of the bisulfite compound would seem to support formula I.

The whole question has been reexamined by Raschig (24), who has shown that the sulfonation of methyl alcohol really produces sodium methyl sulfate. Formula II is thus once more free for formaldehyde sodium bisulfite. Raschig supports his contention by showing that formaldehyde sodium bisulfite readily reacts with ethyl acetoacetate, incidentally affording a convenient route to some rather inaccessible compounds:—



Further, Bazlen (25) in support of Raschig has shown that the hydroxyl

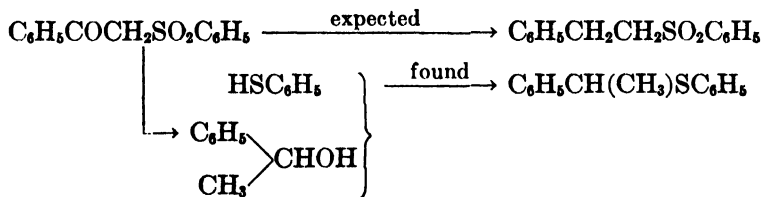
group greatly reduces the strength of the C—S bond so that reduction actually occurs.



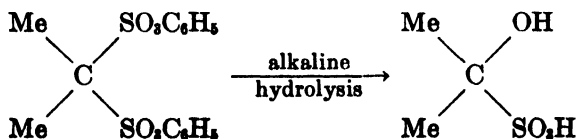
Holmberg (26, 26a) has noted a similar lability in the C—S linkage. Formaldehyde can displace many other (aromatic) aldehydes from their mercaptals. If we postulate that this change is dependent on the reversible formation of mercaptals,



v. Braun and Weissbach (27) offer a very probable explanation of the formation of α -phenylethyl phenyl sulfide by reduction of phenacyl phenyl sulfone (28).



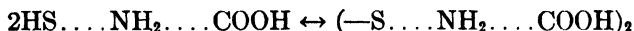
Further, Raschig and Prahl (29) quote Stelling's book "Über den Zusammenhang zwischen chemischen Konstitution und Röntgen Absorptionsspectra," in which it is said that the only formula consistent with Röntgen data is II; moreover Raschig considers that any application of Hinsberg's ideas on the dipolar character of the sulfur atom would lead "zu uferlosen Folgerungen." With all these arguments against formula I Schroeter is in complete agreement, but in his notable work on methiononic acid (30) he encountered an hydroxyisopropylsulfonic acid:



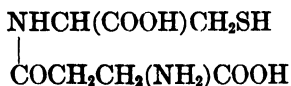
From the nature of its preparation, this substance could not possibly be identical with acetone sodium bisulfite; consequently formula II was also rejected. Raschig, however, in what was unfortunately his final contribution (123), pointed out that Schroeter's analyses (30a) were by no means convincing for a compound of such importance. Consequently the whole subject was reinvestigated by Schroeter (31), and now there is no longer any doubt that neither I nor II adequately represents the bisulfite compounds. We are accordingly compelled to consider formulas of types less familiar in organic chemistry. Of these, a coördination formula has been rather sketchily mooted by Binz (32). Schroeter himself is inclined to regard the bisulfite compounds as polymolecules (33), the constituents R_2CO , SO_2 , and H_2O being held together by electron sharing, not between atoms, but between molecules.

CYSTEINE-GLUTATHIONE

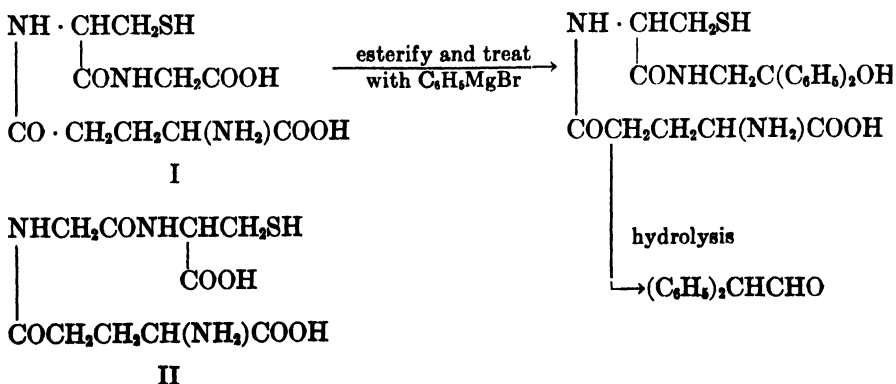
There is much evidence for the idea that the oxidation-reduction processes in living tissue are dependent on an equilibrium.



In 1921, Hopkins (34) isolated glutathione from tissue, and its synthesis by Stewart and Tunnicliffe (35) confirmed the view that it is a dipeptide.



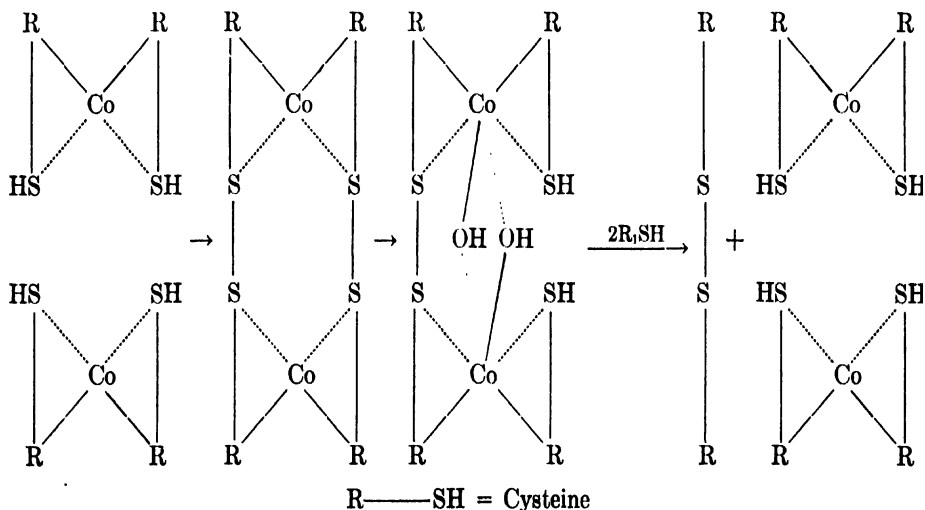
In more recent work, Hunter and Eagles (36) indicated the presence of another amino acid in the extract. Further work by Hopkins (37) and Kendall, Mason, and McKenzie (38) has resulted in regarding glutathione as γ -glutamylcysteinylglycine (I) or glycylcysteine (II),



of which the former is preferred as more readily explaining the production of diphenylacetaldehyde from glutathione ethyl ester hydrochloride by the action of phenylmagnesium bromide.

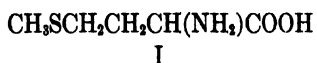
Curiously, this fuller chemical knowledge has resulted in an increasing doubt as to the true physiological function of glutathione, for while the earlier preparations indicated that it could function as a catalyst in the oxidation of the fats and proteins by oxygen, the pure glutathione has now been found to possess this activity only with fats, and even then at an acidity not found in vivo (39).

There seems to be some hydrolysis product of glutathione containing a thiol group which, acting in conjunction with iron, brings about the oxidations formerly attributed to glutathione. Further, in the course of an interesting polarographic study on the activation of hydrogen in the sulfhydryl group in cysteine and glutathione, Brdicka (40) points out that some oxidizing agents, which easily oxidize cobaltous salts and cysteine if they are in common solution, remain without influence on either if they act on them separately. Thus, following Schubert (41), he writes:



In this connection, the investigations of Nicolet (42), Schoberl (43), and McClelland (44) may be particularly mentioned as illustrating the conditions under which simpler disulfides of perfectly definite composition undergo decomposition.

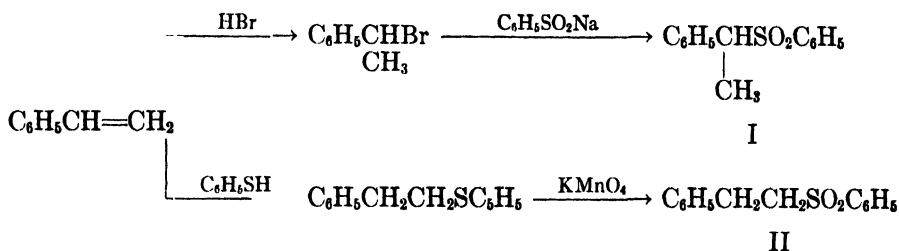
Other cognate nitrogen-sulfur derivatives occur in protein (I) (45) and in wallflower seeds (II) (46).



Mention may also be made here of the mustard oil glucosides which are giving rise to the rapidly developing subject of the sulfur sugars (47, 48).

Addition of sulfur compounds to unsaturated linkages

A striking exception to Markownikoff's rule was discovered by Posner (10). He allowed various unsymmetrical unsaturated compounds to react with thiophenol and oxidized the resulting sulfides to sulfones; in each case the product was different from the sulfone obtained by the action of sodium benzenesulfinate on the hydrobromide formed from the unsaturated hydrocarbon.



It will be noticed that the course of mercaptan addition is implied by non-identity with I rather than by comparison with an otherwise authenticated specimen of II, and while Posner's conclusions as regard styrene have been confirmed and amplified by Ashworth and Burkhardt, other examples which he gave have been shown to correspond neither to type I nor to type II (49), but these discrepancies are probably due to Posner's having handled mixtures of I and II, so that the general accuracy of his scheme is not in doubt.

On the contrary, it receives very important confirmation from the work of Kharasch (9), who shows that the direction of addition of hydrogen bromide to an unsaturated system is controlled by the presence or absence of contaminating peroxide in the unsaturated compound. Thus while pure propylene yields isopropyl bromide, the addition of a trace of benzoyl peroxide results in the formation of propyl bromide.

It seems possible therefore that with those unsaturated compounds which are especially easily contaminated with peroxides arising from their own oxidation, mercaptans first purify the compound and then add on in the "normal" way; whereas with hydrobromic acid the direction of addition is controlled by the contaminating peroxide.

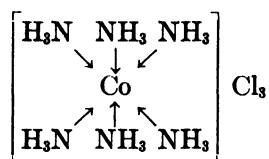
A most ingenious application of the additivity of the thiol group was made by Holmberg (50), who allowed thioglycolic acid to act on rubber and so converted it to an alkali-soluble product.

The work of Mulder (51), Backer (52), and Eigenberger (53) may be consulted on the addition of sulfur dioxide or sulfites to unsaturated compounds.

COORDINATION COMPOUNDS

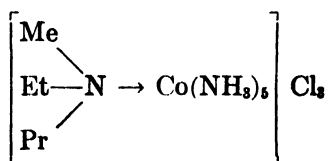
Of the many recent investigations of coordination compounds containing sulfur (125) mention must be made of four which have an important bearing on general chemical theory.

For instance, it is tacitly assumed, although difficult of experimental verification, that the ammonia groups in cobalt hexammine trichloride

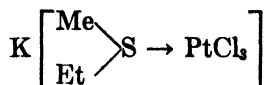


are bound to the central atom by coordination bonds. Now since

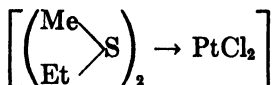
aminoöxides $\begin{array}{c} \text{X} \\ \diagdown \\ \text{Y}-\text{N} \rightarrow \text{O} \\ \diagup \\ \text{Z} \end{array}$ and sulfoxides $\begin{array}{c} \text{X} \\ \diagdown \\ \text{Y}-\text{S} \rightarrow \text{O} \\ \diagup \\ \text{Y} \end{array}$ have been resolved¹
(54, 55, 56),



should be resolvable. Difficulties with the nitrogen compounds led Mann (12) into the sulfur series. Here again was disappointment, for instead of

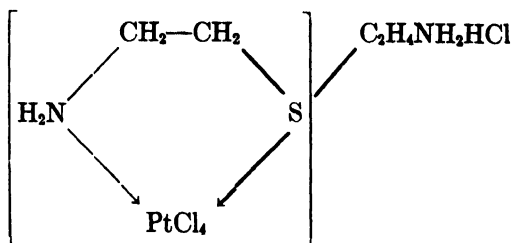


he always obtained



¹ Bergmann does not accept the usual explanation.

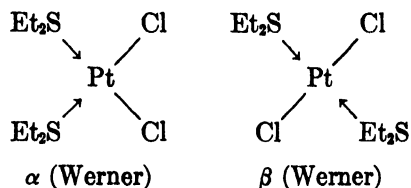
but this was surmounted in the end by preparing



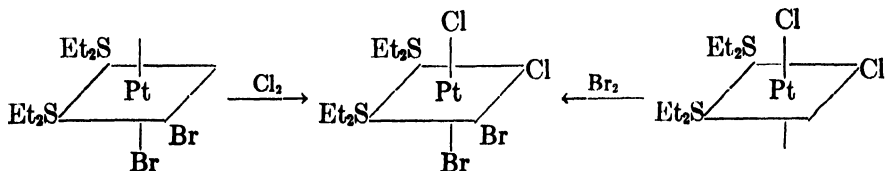
which he resolved with camphor- β -sulfonic acid (the bonds concerned in asymmetry being in heavy type).

It has long been known that salts of the platino series $(\text{Et}_2\text{S})_2\text{PtCl}_2$ exist in two modifications, and various explanations of the isomerism have been proposed (57).

The most important feature of the accepted view is the postulate that the four valencies of platinum lie in one plane



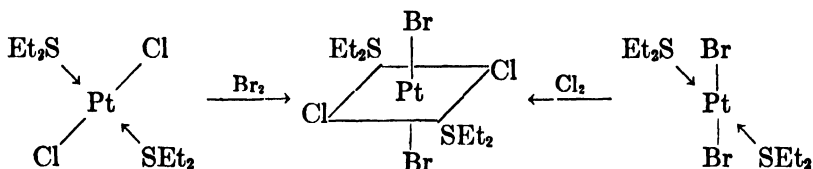
The dihalides are readily converted to tetrahalides in which, as is well-known, the groups have octahedral configuration. Angell, Drew, and Wardlaw (58) found that the α -dichloride reacts also with bromine, and the α -dibromide with chlorine, to yield one and the same dibromodichloride. They interpreted this as indicating a tetrahedral structure for the α -dihalides:—



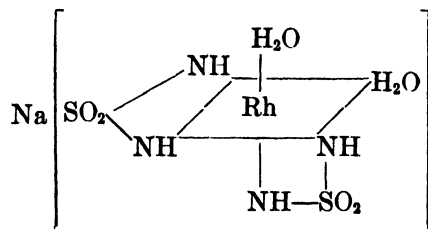
It is obvious that Werner's α -sulfine dichloride should yield a dichlorodibromide *different* from the dichlorodibromide arising from Werner's α -sulfine dibromide.

Without going into the question of the β -series it may be said that severe criticism of their conclusions (59) has impelled Drew and Wyatt

to further work (60), in which they revert to the planar configuration for the α -disulfine by ascribing to it the formula Werner used for the β -disulfine.



One of the final steps in Werner's classic work was the preparation of an optically active cobaltammine containing no carbon atom whatever (61). A second and much simpler example has just been recently reported by Mann (62).



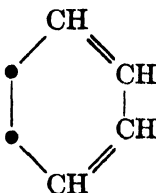
A most interesting dilemma is presented by Manchot and Gall's (63) work on the valence of iron. By the action of nitric oxide on solutions of ferrous sulfate and a mercaptan, they obtained a product A, $\text{Fe}(\text{NO})_2(\text{SR})_2$, which breaks down with formation of a thionitrite $\text{R} \cdot \text{SNO}$ and B, $\text{Fe}(\text{NO})_2(\text{SR})$. Apparently iron is tetravalent in A and trivalent in B, or divalent in A and monovalent in B: "Man kommt also nicht darum herum entwederoder....., eine ungewöhnliche Wertigkeit des Eisens anzunehmen."

An even more critical case of abnormal valency concerns beryllium. In keeping with its covalency maximum 4, many of its salts crystallize with four molecules of water of crystallization. The benzenesulfonates and naphthalenesulfonates are, however, exceptional in having six molecules of water of crystallization (15). Other work of Pfeiffer (16) makes it improbable that this surplus is associated with the negative ion. There is thus the interesting possibility that in these compounds beryllium actually exceeds its covalency maximum.

ISOMERISM AMONG SULFUR COMPOUNDS

The very striking similarity between benzene and thiophene and their derivatives led Hinsberg to suggest (13) that their ring systems must

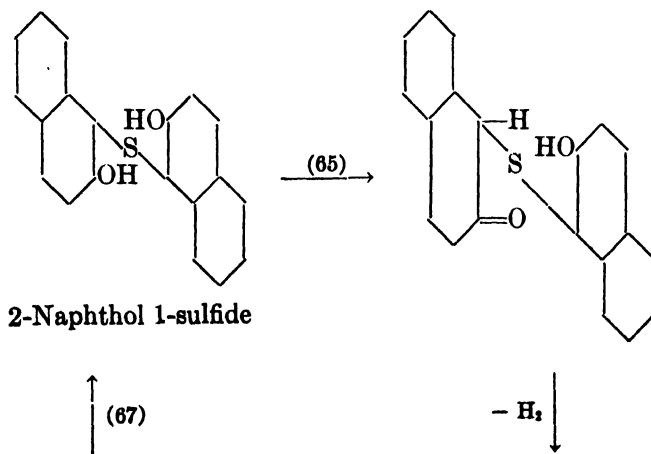
closely resemble each other—that the sulfur atom had two centers from which valency bonds could radiate (88).

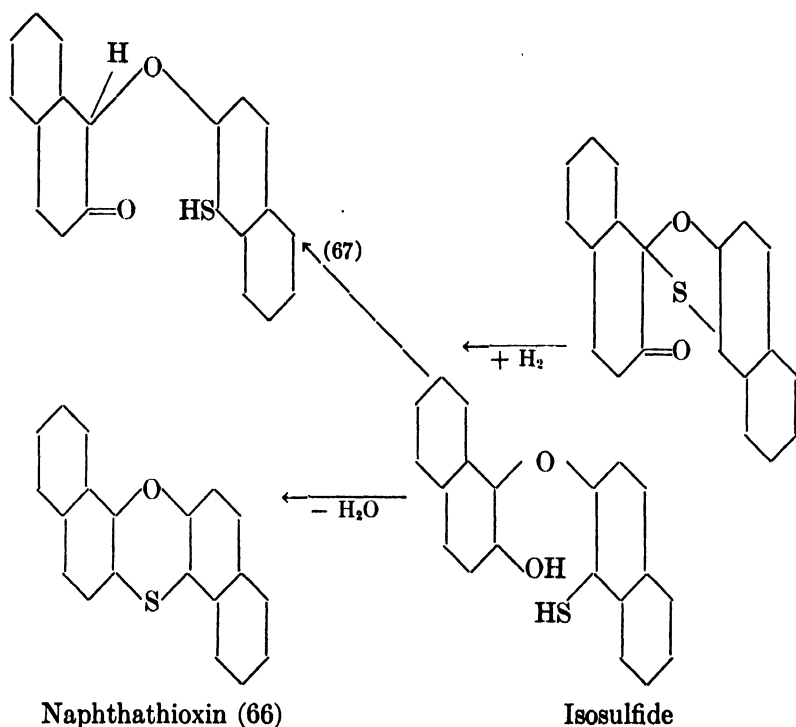


Such a view postulated a suspiciously large number of isomers throughout the compounds of sulfur, and after performing the useful service of directing attention to a variety of actual isomers, it has naturally fallen into discredit with modern views of the atom. In this connection it is interesting to note what remarkably divergent values have recently been proposed for the valence angle of sulfur—the figures ranging from 62° to 146° . Bennett and Glasstone (65) consider that the non-planar configuration of thianthrene indicates that the valence bonds of sulfur adopt an angle of less than 120° . The actual isomers to which Hinsberg's theory directed attention have received other and no less interesting explanation.

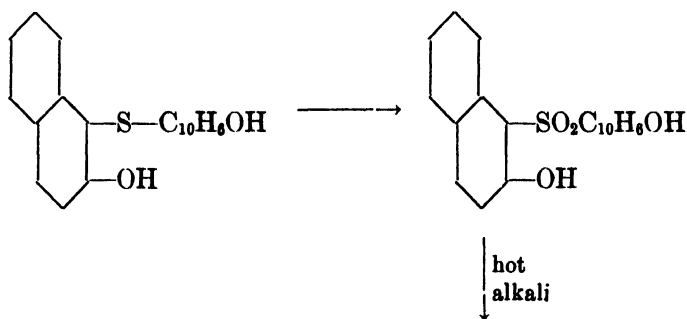
The problem of the existence of two "sulfides" of naphthol, also cited by Hinsberg, has quite a different cause which has required many years to elucidate.

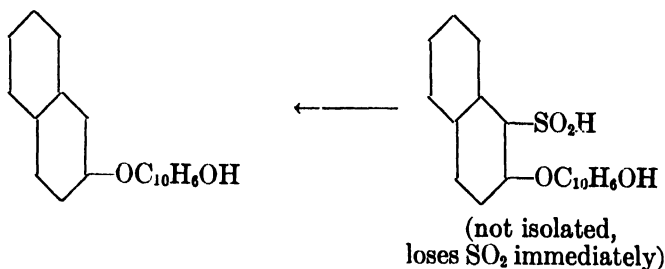
When 2-naphthol 1-sulfide is oxidized, a dehydrosulfide is formed (66), which on reduction yields iso-2-naphthol sulfide, which yields $\alpha,\beta,\beta',\alpha$ -dinaphthathioxin (67) on dehydration, and regenerates 2-naphthol 1-sulfide on treatment with alkali (68). These changes can be formulated:



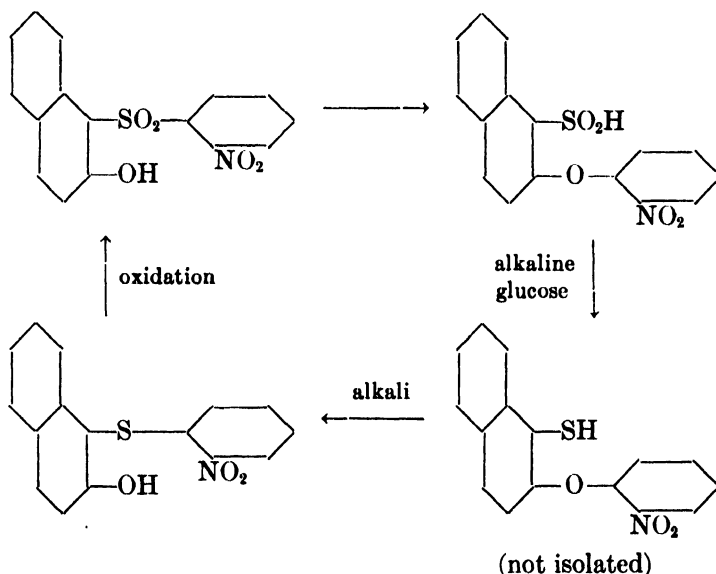


Smiles regards the reconversion of "iso" to β -naphthol sulfide as replacement of the hydroxynaphthyl group from the alpha carbon atom by the more negative thiol group, and he confirms this by showing that when β -naphthol sulfide is oxidized to sulfone with peroxide, the opposite change occurs, for the sulfur atom has assumed a positive character (68). The rearrangement of 2-naphthol 1-sulfone with alkali is unfortunately accompanied by elimination of sulfur dioxide.

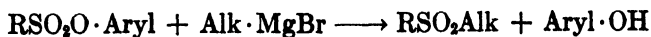




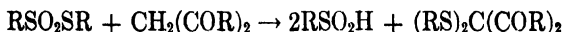
Were it not so, the sulfinic acid (isosulfone) initially produced could no doubt be reduced to "isosulfide" and so a complete cycle realized, as indeed has since been achieved with 2-nitrophenyl-2-hydroxy-1-naphthyl sulfone (69, 70) in which the 2-nitrophenyl nucleus was transferred from sulfur to oxygen and vice versa.



It has long been known that sulfonic esters act as alkylating agents; recently Peacock and Tha (71) have applied them to alkylating malonic esters. Gilman and Beaber (72) have gone one step further and shown that they can, under suitable conditions, even yield hydrocarbons:—

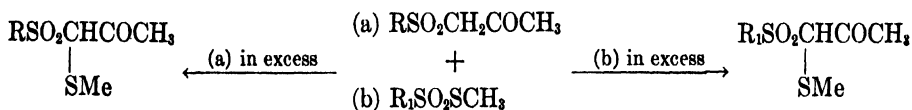


The thiosulfonic esters (formerly called disulfoxides) (73) behave differently for, as Brooker and Smiles showed (74), one can use them to introduce the —SR group into the reactive methylene group.

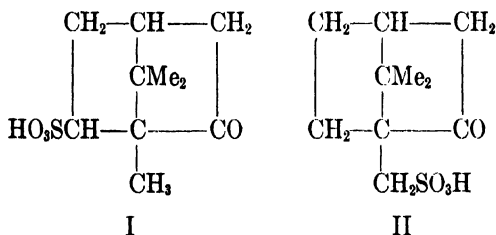


When the methylene group is activated by two sulfonyl groups (bis(sulfonyl)methane) or by one carbonyl and one sulfonyl group (sulfonylacetone) only one hydrogen atom is replaced (75).

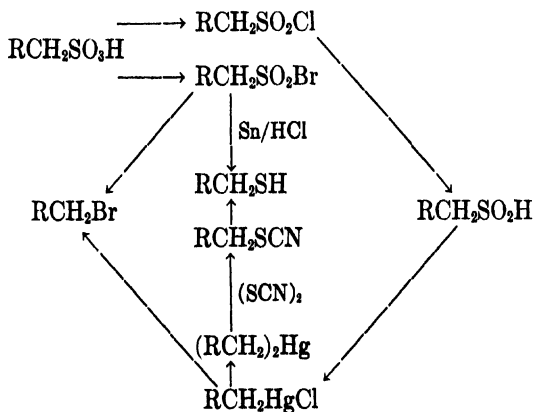
During this substitution the sulfonylacetones are, moreover, subject to an exchange of radicals in a rather unusual way:



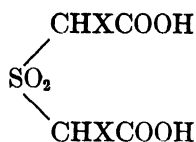
A further peculiarity of this exchange is that it occurs only when an alkyl thio group is the entering substituent (76). From what has just been said, it might seem that in migration of the sulfonyl group the work of Armstrong and Lowry (77) could be reconciled with that of Wedekind, Schenk, and Stusser (78). The former assigned the structure I to Reychler's acid, the latter structure II.



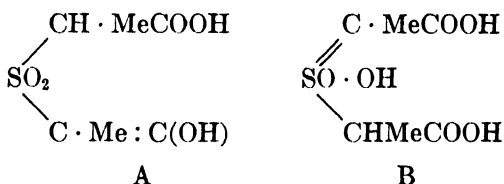
Such, however, is not the case, for Loudon (79), by completing the following cycle under the mildest conditions, was able to show that the substituent remained, as Wedekind, Schenk, and Stusser indicated, in the 10'-position



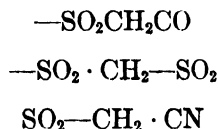
In Sweden the sulfo-fatty acids have received close attention. Ahlberg (80) for instance, has examined the optical activity of acids of the type



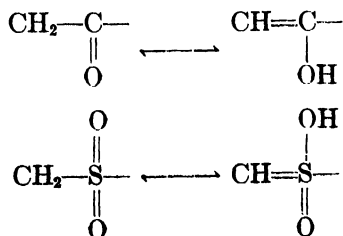
He found that where $X = \text{Me}$ the acid is so readily racemized as to be incapable of isolation in the active condition, but with $X = \text{Et}$ or isopropyl, the active acid is readily obtained. He considered that the racemization was due to the tautomeric changes represented by either A or B:



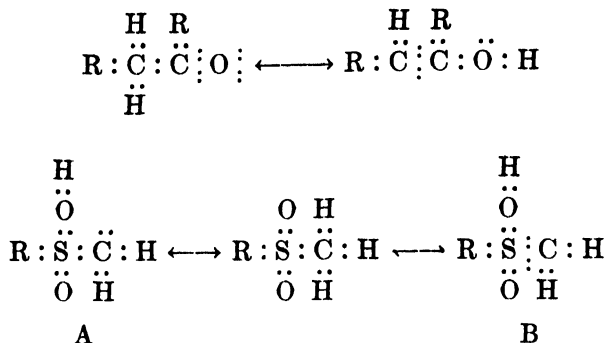
He preferred B and suggested that the efficacy of the higher alkyl groups was to be explained on the basis of a steric hindrance effect in the 1,5-position (ethyl). Now, because compounds containing the groupings



dissolve in alkali, are readily methylated, and give compounds with diazobenzene chloride, Hinsberg and others (81, 81a, 81b) extended the idea of enolization to the sulfone group.



Expressed in that way, it did no obvious violence to the existing ideas of valence; but on the modern electronic conception it is evident that the sulfonyl group has quite another character from the carbonyl.

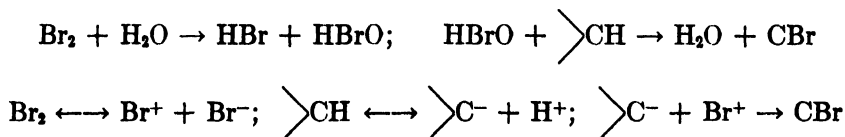


The "enolization" of the sulfone group leads either to the establishment of a lone pair of electrons on the carbon atom (formula A), or to the sulfur atom being surrounded by ten electrons (formula B) (18).

The former alternative would not involve any movement of electrons, but it would lack driving force, for the proton would be leaving an atom to which it is firmly attached (carbon) to take up its position on one to which its attachment is much looser (oxygen) as, e.g., the strength of sulfuric acid indicates.

Since in methylene disulfones, where only one electronic arrangement is possible, the electron system of the anion must be identical with the free hydrogen compound, these salts are C-salts in this sense that the anionic charge corresponds to a lone pair of electrons on the carbon atom. That means there is no binding between metal and carbon comparable to that in an organometallic compound. Unlike the aliphatic diazo compounds which also have a lone pair of electrons on carbon, these polysulfonyl salts are colorless, because the lone pair is so firmly bound.

Another point of interest is the behavior of methylene disulfones on bromination in aqueous solution. As is well-known, acids promote the bromination of such compounds as acetylacetone. The effect with the sulfur derivatives is quite the reverse; this leads Arndt and Martius to postulate their bromination occurring by either (or possibly both),



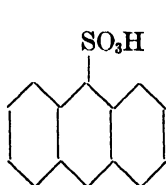
for, evidently, both processes would be retarded by acid.

This real difference between carbonyl and sulfonyl accounts for the resistance of methanesulfonyl chloride to chlorination (82) and is also perhaps the reason why chloriodomethanesulfonic acid (83) can be ob-

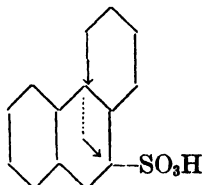
tained optically stable while chloriodoacetic acid has not been resolved (126).

We are thus obliged to reject Ahlberg's explanation (B) of the optical instability of sulfodipropionic acid, and the fact that sulfopropionic acid has been resolved (84) rather speaks against his alternative formula (A) as he himself admits.

Another rearrangement recently described by Schroeter and Gotzsky (85) resembles these involving the migration of a sulfonyl group.

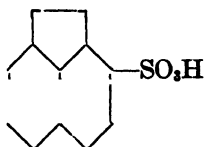


Octhracenesulfonic acid

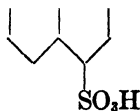


Octanthrenesulfonic acid

Likewise, the sulfonation of acenaphthene may yield either X or Y.

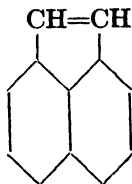
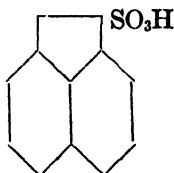


X



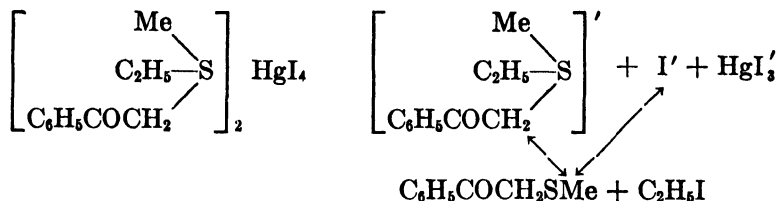
Y

Each of these undergoes rearrangement on fusion with alkali, the final product being acenaphthylene.

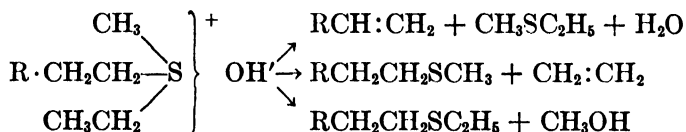


Sulfonium salts

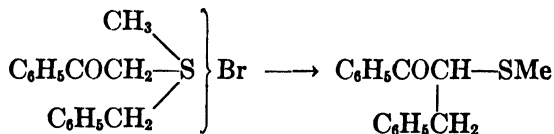
These are in many ways similar to quaternary ammonium salts. Thirty years ago representatives of each class were resolved, and problems which arose then (92) are still attracting interest (93). The ready racemization of sulfonium mercuriodides has, for instance, recently been shown to depend on a reversible decomposition of the ions:—



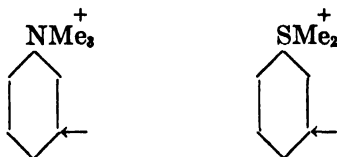
The thermal decomposition of sulfonium hydroxides has been found by Ingold, Jessop, Kuriyan, and Mandour (87) to be quite parallel to that observed with ammonium hydroxides.



Even more interesting is Stevens' discovery that with phenacylbenzyl-methylsulfonium bromide a transformation of a type first observed by himself (96) in the ammonium series can be realized (97).



The similarity between ammonium and sulfonium salts extends to aromatic substitution, both groups being powerfully meta directing (89, 90, 91).

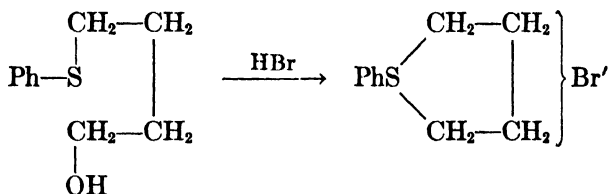


On the other hand, it is by no means obvious that the suppression of basic characteristics in pyrrole and thiophene has as yet been satisfactorily explained (122); although it may be true that in pyrrole the lone pair of nitrogen electrons is absorbed in an aromatic sextet, since the sulfur atom in thiophene has *two* lone pairs, one of these, on the above theory should remain and so give rise to a methiodide or a sulfoxide, which, as a matter of fact, has never been observed. A valuable paper by Richardson and Soper (98; also 99) indicates that the combination of a bromide and a sulfide to form sulfonium bromide should be greatly facilitated by use of

a solvent of high cohesion, e.g., nitromethane.² Application of this important solvent enabled Ingold and Jessop (100) to isolate fluorenyl-9-dimethylsulfonium bromide, but it is by no means certain that their interpretation of the subsequent degradation of this compound is fully established.

It is well-known that many substances which show no other basic characteristics will form salts with perchloric acid. Following this up Hinsberg has recently subjected diphenyl sulfide, dibenzyl sulfide, and di-*n*-butyl sulfide to the action of hot perchloric acid, and in each case claims to have isolated an isomeric sulfide. It is unfortunate that these seem rather ill-defined unstable bodies (94, 95).

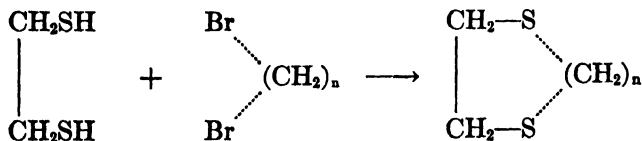
An interesting example of the transmission of the influence of a sulfur atom directly through space rather than along the intervening chain of atoms is provided by Bennett and Mosses' (21) discovery that phenyl δ -hydroxybutyl sulfide is convertible to the cyclic sulfonium bromide under conditions that scarcely affect the γ -hydroxypropyl or ϵ -hydroxyamyl sulfides:—



Phenyl δ -butyl sulfide

NEW CYCLIC TYPES

It has long been known that in the preparation of cyclic sulfides, such as dithiane, more or less of the material is converted to high molecular polymers (101). These, which have usually been removed and considered as loss, have now been investigated by Tucker and Reid (102).

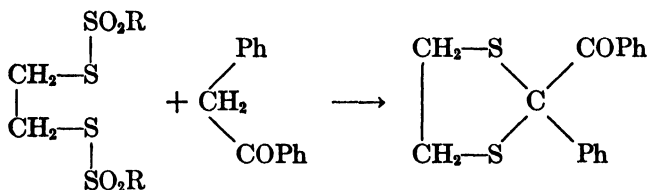


where *n* is 1, 2, 3, 4, 5, or 6. They find that in every case the polymers

² Attempts to prepare thiophenesulfonium derivatives in nitromethane were, however, unsuccessful, and yet this cannot be attributed to inherent instability, for Backer and Strating (127) have quite recently isolated the sulfones of methylated thiophenes by combining butadienes with sulfur dioxide.

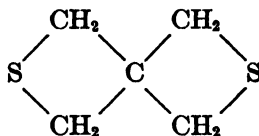
can be degraded to dithiane by heating with ethylene bromide or, in some cases, with hydrogen chloride.

Similar ring systems have also been prepared by Chivers and Smiles (103),

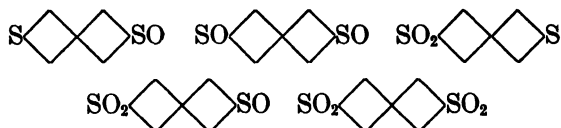


and Gibson (104) has found evidence that the unsubstituted 1,3-dithiolane can give rise to a ψ base.

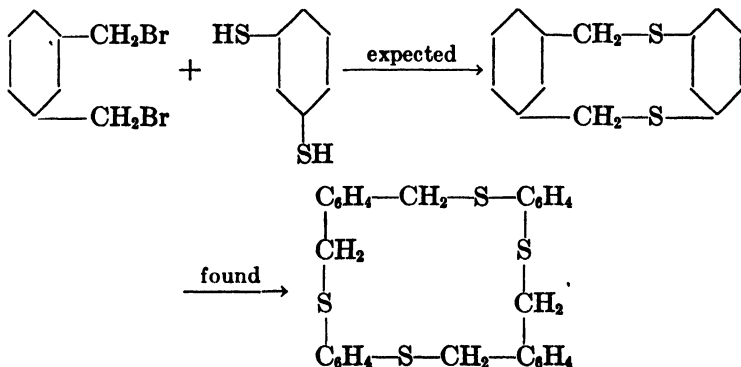
A most interesting spiro cyclic type has just been isolated by Backer and Kenning (105). They find that pentaerythritol tetrabromide reacts very easily with potassium sulfide to give



which is stable enough to allow of the isolation of the five expected oxides



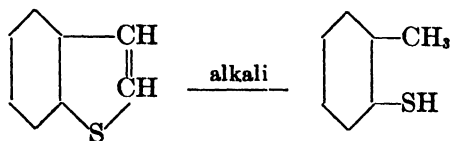
and of being brominated without rupture of the spirane system. On the other hand Reindel and Schuberth (106), attempting to make ten-membered rings from meta-substituted benzenes, obtained only polymeric products.



In investigating a number of cases where ring closure may take place to

form either a nitrogen or a sulfur ring compound, Arndt and Bielich (107) find that in neutral or acid media the heterocyclic member is sulfur; in alkaline media it is nitrogen.

The reverse process, the rupture of a sulfur ring compound, has been developed by Weissberger and Seidler (108) as a valuable method for removing thionaphthene from naphthalene.

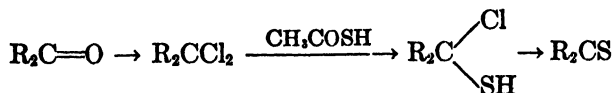


SACCHARIN

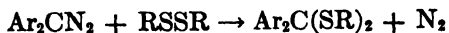
Although it is nearly fifty years since saccharin was discovered, the secret of its sweetness is still unexplained. Various attempts on the lines of "glucophores" and "auxoglucs" have met with little success. The fact that very concentrated solutions are relatively less sweet than the more dilute led Magidson and Gorbatschow (109) to suggest that as saccharin is an acid, its sweetness bears a direct relationship to its degree of dissociation. They attribute a bitter taste to the undissociated molecule, but although they bring forward some evidence in support of their contention, Tafel and Wagner consider it inconclusive.

THIOKETONES

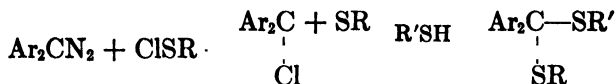
During the last few years Schönberg has made an exhaustive study of thioaldehydes and thioketones. He finds (110) that those constitutional changes which favor or inhibit the existence of free "triarylmethyl" groups also favor or inhibit the tendency of thioketones to polymerize; and likewise that those changes which favor or inhibit the dissociation of hexaaryl ethanes also favor or inhibit the dissociation of polymerized thioketones. Thus while thioformaldehyde and thiobenzaldehyde are known only trimeric, thiobenzophenone exists only monomeric. The existing routes to thioketones being of rather restricted applicability, it is of interest to mention that a more general route has now been devised (111).



The corresponding mercaptides are accessible from diaryldiazomethanes,

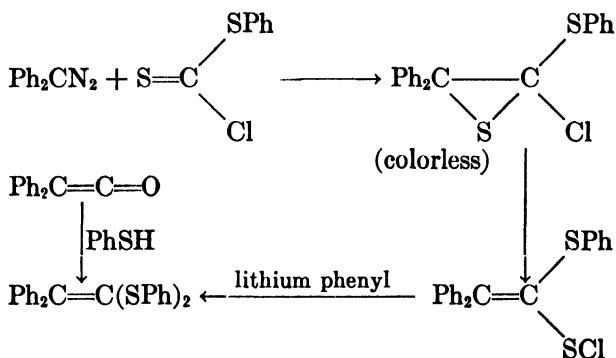


and also the unsymmetrical mercaptides by using aryl sulfur chlorides (112).

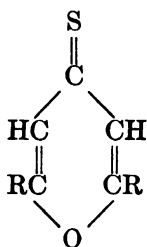


The necessary aryl sulfur chloride is readily obtained, according to Lecher and Holzschneider (113), by adding the mercaptan to a solution of chlorine (not vice versa).

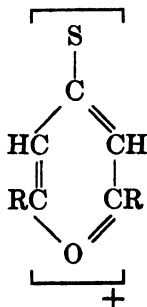
Substituted diazomethanes also react with chlorothiocabonic esters; in examination of such a reaction Schönberg and Vargha (114) detected a most unusual rearrangement and most ably substantiated their explanation.



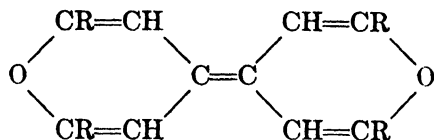
Arndt, Scholz, and Nachtwey (115) find that thioketones of the type,



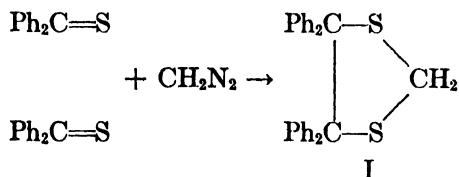
can also exist in the form



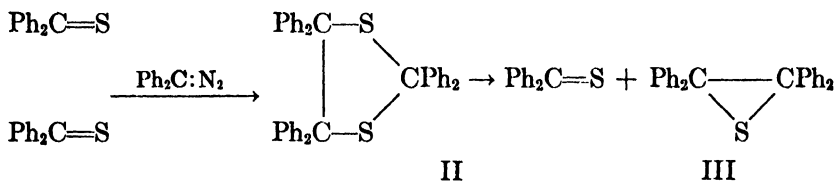
Where R is an acidifying substituent (C_6H_5 or COOEt), the true thioketone form is favored, as is shown by the readiness with which it decomposes to give sulfur and



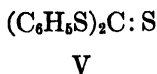
These substances are not only thermolabile, but extraordinarily sensitive to what one might consider slight changes in constitution. Thus while thiobenzophenone reacts with diazomethane to give a relatively stable 1,3-disulfide,



the corresponding product from diphenyldiazomethane is easily decomposed with regeneration of half of the thiobenzophenone.



The regenerated thiobenzophenone undergoes reaction afresh with diazodiphenylmethane, and so on until all is converted to tetraphenylethylene sulfide. Even more sensitive are the products from diphenyl trithiocarbonate (V),

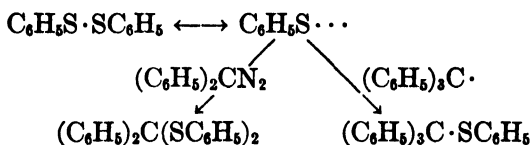


for with diazomethane it gives a 1,3-disulfide analogous to II, while with diazoethane it breaks down as $\text{II} \rightarrow \text{III}$ (116, 117).

Monovalent sulfur

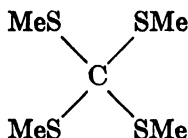
The question whether disulfides are capable of dissociating into free radicals with monovalent sulfur was examined by Lecher, who came to the conclusion that they were not (118). Schönberg, Rupp, and Gumlich

(119) now show that his experimental technique was not sensitive enough, and that with suitable reagents diphenyl disulfide shows all the characteristics of dissociation.



Admittedly, solutions of diphenyl disulfide are stable to oxygen, and the extent of dissociation is too small to be detected by molecular weight measurement, but Beer's law is not obeyed, and some more complicated disulfides decolorize metal-ketyl solutions practically instantaneously (22).

In direct contrast to such supra-activity there is tetramethylthiomethane



which has been isolated, after many failures, in the Groningen laboratory. It is quite remarkable for an inertness reminiscent of sulfur hexafluoride (121).

Modern microcombustion methods greatly simplify the analysis of sulfur compounds. For compounds containing carbon, hydrogen, and sulfur only, Pregl's combustion method over platinum followed by titration is so simple and speedy that it leaves little to be desired. For compounds which contain nitrogen and for halogen as well, Friedrich (120) has devised a satisfactory modification.

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